Scope, Application and Mechanistic Details of the Nickel-Catalyzed *Z*-Selective Isomerization of Terminal Olefins

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Frankenberg (Eder)

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E. I. Grigoryev, F. Weber, G. Hilt, R. Berger, *Org. Chem. Front.* **2018**, submitted.
"*Mechanism and Selectivity of the Rare Cobalt(I) and Nickel(I)-Catalysed Isomerisation of Terminal Alkenes*."

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"*Synthesis of Non-Conjugated Trienes via in situ Hydrovinylation/Wittig-Olefination of Unsaturated Phosphonium Salts*."

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"*Structure-Dependent Nickel-Catalysed Transposition of N-Allylamides to E- or Z-Enamides*."

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"*Nickel-Catalyzed Double Bond Transposition of Alkenyl-Boronates for in situ syn-Selective Allylboration Reactions.*"

F. Weber, A. Schmidt, P. Röse, M. Fischer, O. Burghaus, G. Hilt, *Org. Lett.* **2015**, *17*, 2952-2955.
"*Double Bond Isomerization - Highly Reactive Nickel Catalyst Applied in the Synthesis of the Pheromone (9Z,12Z)-Tetradeca-9,12-dienyl Acetate*."

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„With your best pals around, you're never in it alone.“

– Winnie Puuh

für Opa Wilhelm

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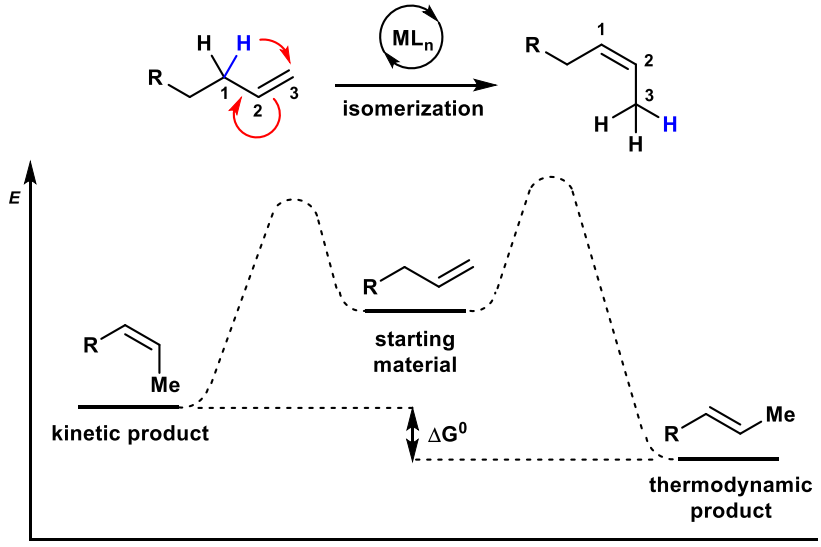
1. Introduction

1.1 Isomerization of Terminal Olefins to 2-Alkenes

The isomerization of unsaturated substrates constitutes as an atom-economic alternative to conventional double bond forming processes, such as carbonyl olefination,[1] alkyne reduction,[2] cross-coupling reactions,[3] or olefin metathesis.[4] The translocation of a terminal double bond can be considered as a formal 1,3-hydride shift, for which a defined stereocontrol of the resulting double bond is the biggest challenge. As depicted in Scheme 1, the *E*-configured olefin is the thermodynamically favored product, whereas the *Z*-configured isomer is predominantly formed under kinetic control.[5]



Scheme 1: Energy diagram for the isomerization of terminal alkenes to the kinetic (*Z*-olefin, left) and thermodynamic product (*E*-olefin, right), (*E* = energy, ΔG^0 = Gibbs energy).

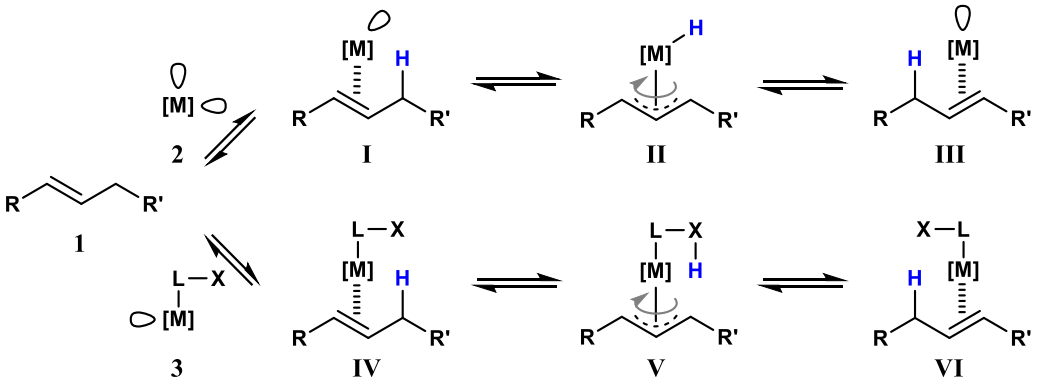
Several different methods to realize an isomerization process have been described in the literature.[6] This work focusses on the transition metal-catalyzed migration of a terminal double bond, which provides access to unsaturated target molecules with exactly defined double bond configuration and location. The double bond transposition can occur *via* different pathways.[7] The understanding of the mechanism for olefin isomerization is meaningful to illustrate the complexity of this supposedly simple reaction.

1.1.1 Mechanistic Insights

All steps corresponding to the movement of a double bond are reversible. Consequently, the thermodynamic ratio of alkenes is reached when the metal species remains active for an

adequate time.[8] When an irreversible step occurs at a certain position, kinetic factors have to be considered. In the following, two mechanistic pathways will be presented in more detail: The allyl (1,3-hydride shift) and the alkyl (1,2-hydride shift) mechanism.[9]

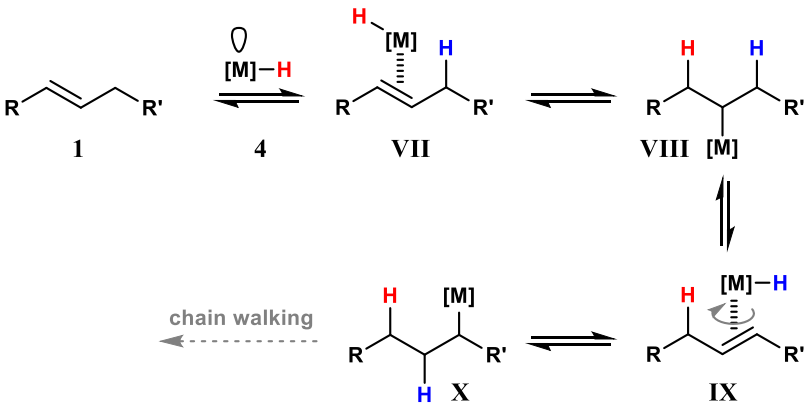
When the hydride transfer is provided from the substrate's activated allylic position the allylic pathway occurs *via* formal 1,3-hydride shift through either an inner or an outer sphere mechanism. As depicted in Scheme 2, the inner sphere mechanism needs 14-electron metal complexes **2** with two vacant coordination sites.[8,10]



Scheme 2: Allyl pathway of the 1,3-hydride shift with inner (top) and outer sphere mechanism (bottom).[8]

After formation of the η^3-allyl complex **II** through reversible oxidative addition and rotation, the reductive elimination provides the translocated olefin metal complex **III**. The hydride (highlighted in blue in Scheme 2) is transferred from the activated allylic position of alkene **I**. The outer sphere mechanism has to be considered when the ligand acts as base (with X = N or O) and enables deprotonation of the allylic position of **IV**.[8,11,12]

Most reports in literature describe the isomerization proceeding through a metal hydride species **4** formed by initial activation, for instance, through addition of a hydride salt or complex.[13,14]



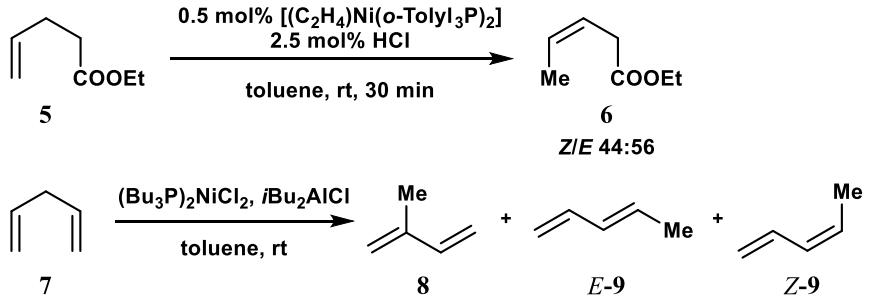
Scheme 3: Alkyl pathway of the 1,2-hydride shift.[8]

In the alkyl mechanism in Scheme 3, a metal hydride species **4** with a vacant coordination site is required for migratory insertion. The insertion of the olefin into the [M]–H bond usually takes place through a four-centered transition state leading to an alkyl metal species **VIII**. The following *β*-hydride elimination furnishes the isomerized olefin π-complex **IX**, which undergoes rotation and hydrometalation to **X**. The oxidation state of the metal does not change during the process. The *Z*/*E* ratio of the outcoming alkene typically depends on thermodynamic stability or nature and ligand sphere of the metal.[15] In case of the hydride mechanism, another insertion can take place letting the metal hydride walk through the chain. Therefore, the biggest challenge is the realization of a double bond transposition over exactly one position without further chain-walking. Several approaches can be found in the literature.[16–18,19]

Since these reactions are often catalyzed by precious metals, a growing demand in the utilization of first-row transition metals has increased. They are an attractive alternative to their higher homologues due to their high abundance, lower cost and high reactivity. In recent years, several first-row transition metal catalysts, especially iron-, nickel- and cobalt-based systems, have been described for a targeted isomerization over one position. The following chapter will thus be focused on the stereoselective isomerization of unfunctionalized alkenes as well as the double bond translocation in allylic systems through first-row transition metal catalysis.

1.1.2 Isomerization of Unfunctionalized Alkenes via First-Row Transition Metal Catalysis

Already in the 1970's Miller and Lochow described the first nickel-based catalyst system comprising ethylenebis(tris-*o*-tolylphosphite)nickel(0) and HCl used for the isomerization of homoallylic ester **5** to a *Z*/*E*-mixture of crotylester **6** (Scheme 4, top). For skipped dienes **7** they used $Ni(Bu_3P)_2Cl_2$ in combination with the Lewis acid iBu_2AlCl (Scheme 4, bottom).[20]

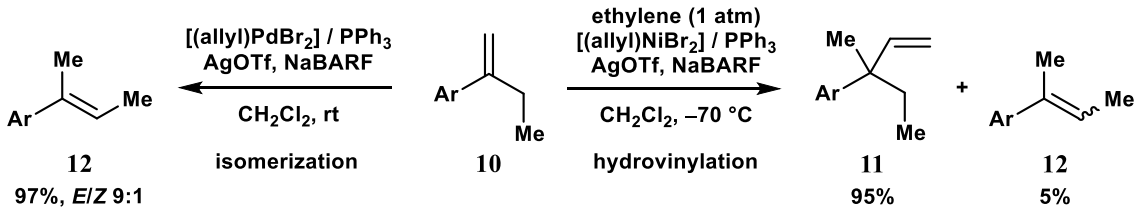


Scheme 4: Nickel-catalyzed isomerization of simple 1-alkenes and diene structures.

Another *Z*-selective isomerization of 1-pentene was described by Kanai in the early 1980's. They explained the double bond transposition proceeding *via* metal hydride species. The

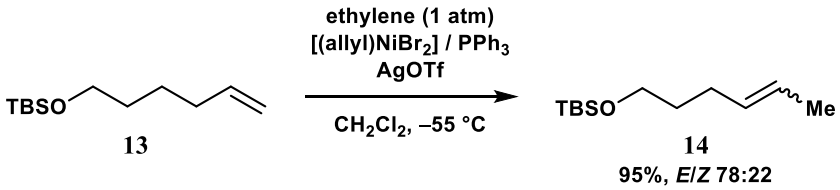
addition of the Lewis acid $SnCl_2$ facilitated the reaction through halide abstraction from the catalyst precursor $Ni(PPh_3)_3Br$. They further suggested that the active catalyst species is a Ni(I) species formed by *in situ* reduction with Zn.[21]

In a 2009 report, RajanBabu *et al*. observed the transposition of an exo-double bond as side reaction during their investigations on a nickel-catalyzed hydrovinylation of exocyclic alkenes of type **10** (Scheme 5) and ethylene to terminal alkenes (**11**) using a catalyst system comprising [(allyl)$NiBr_2$] and triphenylphosphine. They wondered whether the hydrovinylation conditions could be modified towards a selective isomerization of the 2,2′-disubstituted alkene to trisubstituted alkene **12**. After detailed optimization they could get access to products with an *E*-configured trisubstituted double bond. Compared to the nickel precursor, they found out that the neighboring palladium catalyst shows enhanced reactivity. Likewise, they propose a metal hydride mechanism for the isomerization using silver triflate for halide abstraction.[22]



Scheme 5: Isomerization as side reaction observed by RajanBabu (Ar = 4-chlorophenyl, BARF = tetrakis[3,5-bis(trifluoromethyl)-phenyl]borate).

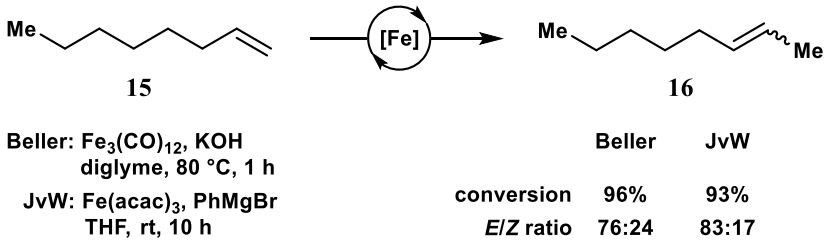
For substrates with an allylbenzene substructure the double bond migration is always limited to one position.[23] If the (homo)allylic position of the carbon chain in the product is unsubstituted, another isomerization can take place. For linear substrates, for instance silyl ether **13**, [(allyl)$NiBr_2$] / PPh_3 proved to be the more reactive catalyst, leading to mainly *E*-configured 2-alkene **14**. The reaction had to be performed at temperatures as low as –55 °C in order to suppress further 1,3-hydride shifts and to guarantee the stability of the nickel catalyst.[22]



Scheme 6: Nickel-catalyzed isomerization to 2-alkenes by RajanBabu.

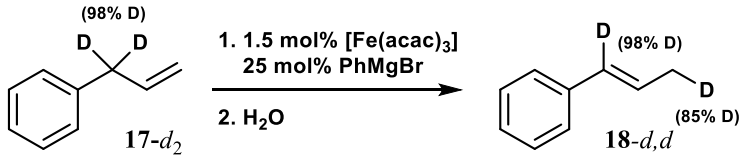
Additionally to nickel, the iron-catalyzed isomerization is numerously presented in literature.[24] Mechanistically, the iron-mediated 1,3-hydride shift supposedly proceeds through an iron hydride intermediate.[25] In 2011, Beller and Jacobi von Wangelin (JvW in Scheme 7) used an iron-based catalyst system for the isomerization of unfunctionalized 1-alkenes (1-octene, **15**)

obtaining 2-octene (**16**) in moderate to good *E*-selectivity. Beller postulated a trinuclear iron hydride complex as active species. The selectivity is described by the high steric demand of the catalyst.[26,27]



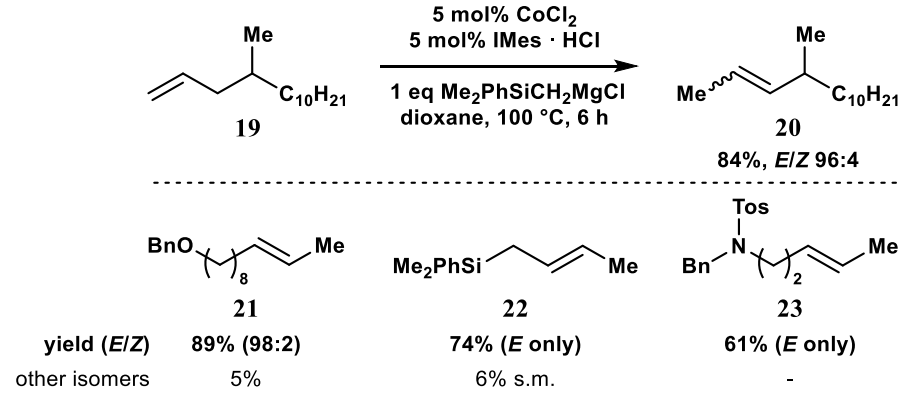
Scheme 7: Iron-catalyzed isomerization of simple terminal olefins to 2-alkenes (acac = acetyl acetonate).

Jacobi von Wangelin *et al*. proposed an allylic pathway for their Grignard-assisted isomerization. They could prove it by deuterium labeling experiments figuring out that the allylic position of deuterated allylbenzene (**17**-d_2) is the origin of the deuteride located at the methyl group in the product **18**.[26] Scheme 8 illustrates the experiment.



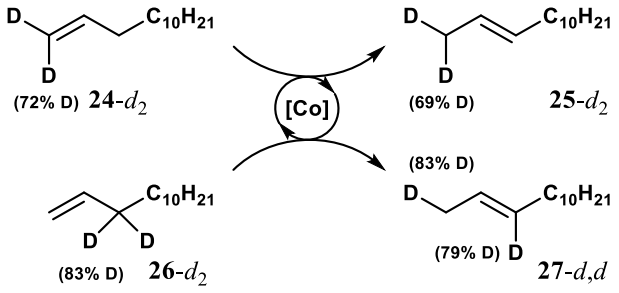
Scheme 8: Deuterium labeling for the iron-catalyzed isomerization *via* allylic pathway.

For a targeted isomerization of terminal olefins to 2-alkenes, the first cobalt-based catalyst was described by Oshima *et al*. in 2009 providing access to mainly *E*-configured alkenes (**19** → **20** in Scheme 9). Similar to Jacobi von Wangelin's report, a Grignard reagent was necessary for the reduction of the Co(II)-precursor. Unfortunately, they did not mention whether the active catalyst is a Co(I) or Co(0)-species. Substrates with simple alkyl chains (**20**), ethers (**21**), silanes (**22**) and even a protected tertiary amine (**23**) were well-tolerated by the catalyst.[28]



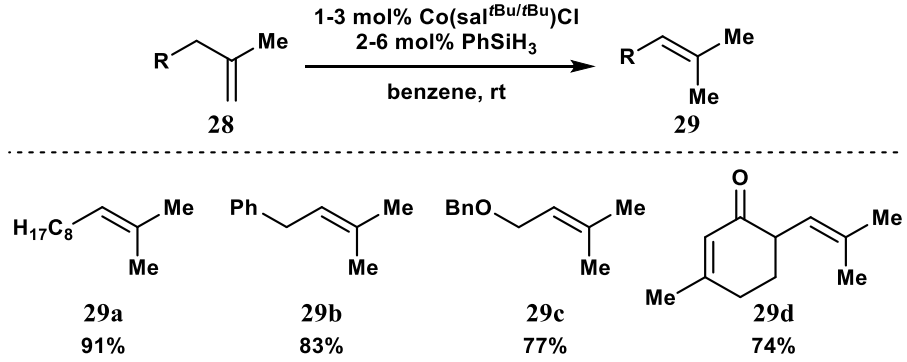
Scheme 9: Cobalt-catalyzed isomerization to 2-alkenes by Oshima (s.m. = starting material, IMes · HCl = 1,3-bis(2,4,6-trimethylphenyl)imidazolium chloride.

For the formal 1,3-hydride shift, Oshima suggested a mechanistic pathway upon cobalt hydride formation, which could also be underlined by deuterium labeling experiments. Two deuterated substrates were subjected to the reaction. As can be seen in Scheme 10, terminally deuterated tridec-1-ene (**24**-d_2) was isomerized leaving the isotopes untouched at the terminal position (**25**-d_2) while the internally deuterated tridec-1-ene (**26**-d_2) was isomerized with the expected transposition of one deuteride from the allylic to the terminal position of **27**-*d*,*d*.[28]



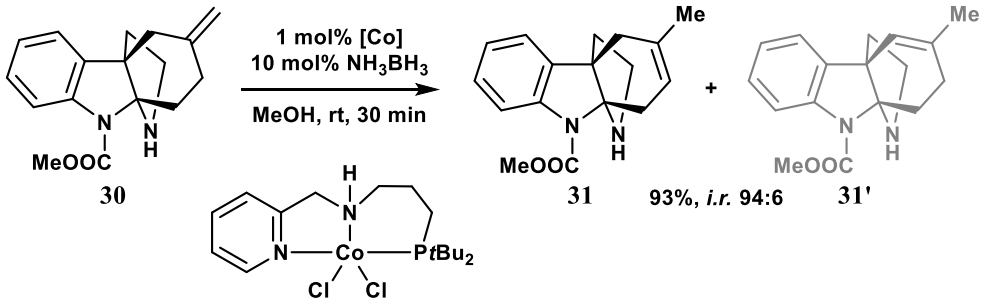
Scheme 10: Deuterium labeling to confirm the proposed 1,3-deuterium shift.

Another cobalt-catalyzed isomerization of olefins **28** with an *exo*-double bond was described by Shenvi *et al.* in 2014. They proposed a radical isomerization *via* reversible hydrogen atom transfer (HAT) predominating hydrogenation as possible side reaction. They used a cobalt(III)-salen precursor with phenylsilane as hydride donor gaining access to *E*-configured 2-alkenes **29** with trisubstituted double bonds without defined stereoselectivity (Scheme 11).[29]



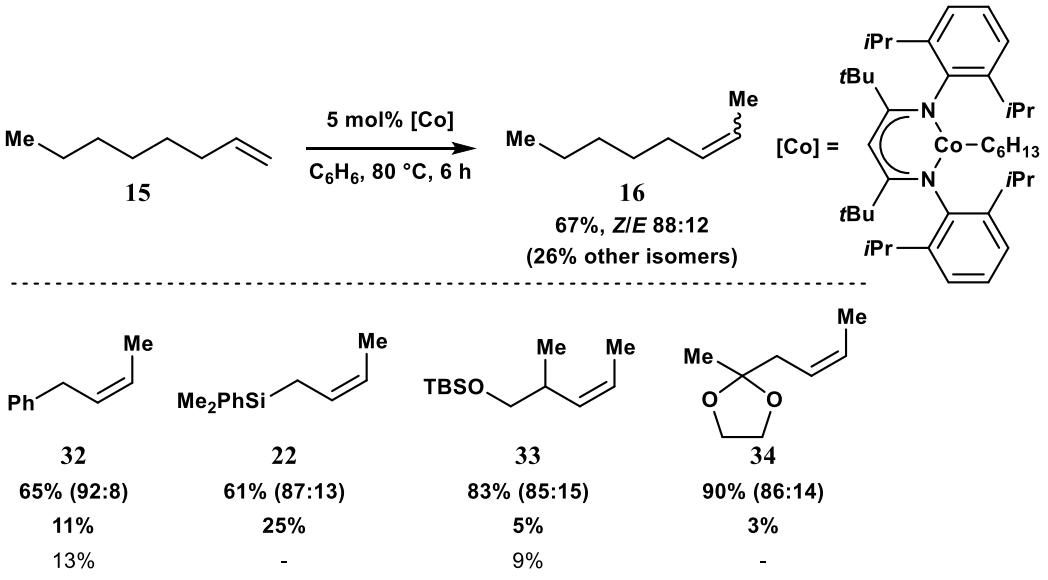
Scheme 11: Cobalt-catalyzed isomerization of exo-double bonds to trisubstituted alkenes (sal$^{tBu/tBu}$ = (*R*,*R*)-(–)-*N*,*N*′-Bis(3,5-di-*tert*-butylsalicylidene)-1,2-cyclohexanediamin).

This year, Liu and coworkers could realize a *Z*-selective monoisomerization of either γ-substituted terminal alkenes or 1,1-disubstituted olefins like tetracycle **30** using a cobalt-based catalyst system with NNP-pincer ligands shown in Scheme 12. Ammonia borane was used as reducing agent and hydride source. In case of non-cyclic olefins, an isomeric excess (*ie*) of up to 60% was possible. Besides utilization for a broad alkene scope, including a derivatization of testosterone, they used their method as key step for the total synthesis of the indole alkaloid minfiensine (**31**).[30]



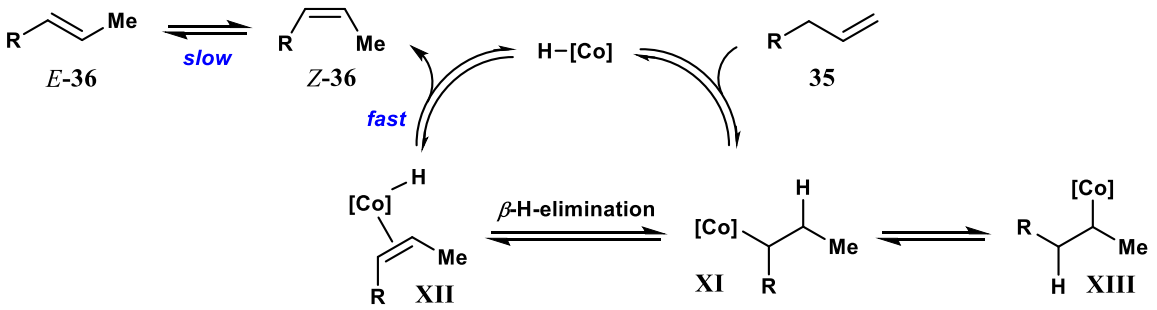
Scheme 12: Liu's cobalt-catalyzed isomerization as key step in the synthesis of minfiensine (*i.r.* = isomeric ratio).

In 2014, Weix and Holland found a high-spin Co(II)-catalyst suitable for the double bond transposition over exactly one position in linear substrates without adjacent functional group. They suggested the bulky *β*-diketiminate ligand having the appropriate kinetic selectivity for the formation of predominantly *Z*-configured 2-alkenes, for instance 2-octene (**16**), with a *Z*/*E* ratio of 88:12. Their approach, shown in Scheme 13, is the first *Z*-selective isomerization by a cobalt catalyst reported in literature achieving *Z*/*E*-stereoselectivity of up to 92:8 in good yield.[31]



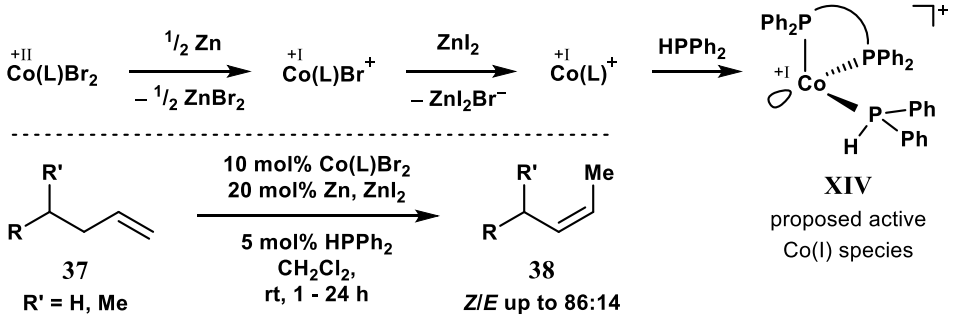
Scheme 13: Cobalt-catalyzed *Z*-selective isomerization by Weix (s.m. = starting material).

Due to the metal hydride walking through the chain, the formation of undesired higher homologues was also observed (up to 13% in case of 2-alkene **32**). Weix *et al*. explained that the amount of *E*-configured 2-alkene increased over time, so that the reaction had to be quenched when the amount of 2-*Z*-isomer has reached its maximum. The *Z*-selectivity is determined by insertion product **XI** in Scheme 14. Elimination of the *Z*-alkene occurs more rapidly than the reversible *Z* to *E* isomerization (*Z*-**36** to *E*-**36**) which indicates that this step is kinetically controlled.[31]



Scheme 14: Origin of the *Z*-selectivity of the isomerization by Weix.

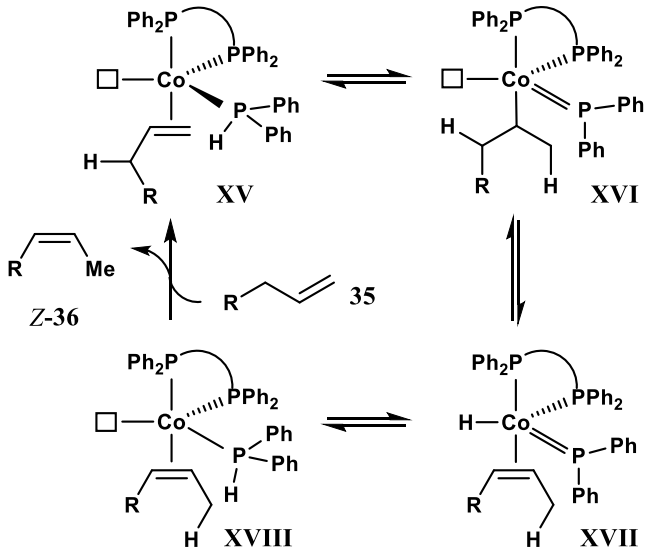
The same year, our group developed a similar *Z*-selective isomerization where the double bond migration is limited to only one position (**37** → **38** in Scheme 15, bottom). The sum of other internal isomers for most of the substrates was less than 1%. Our cobalt catalyst system consists of the Co(II)-precursor with a bidentate phosphine ligand, Zn powder as the reducing agent and the Lewis acid ZnI_2 for halide abstraction from the active Co(I)-species **XIV** (Scheme 15, top). The addition of diphenylphosphine is crucial in terms of *Z*-selectivity as well as reactivity.[32]



Scheme 15: Formation of the proposed active Co(I) species (top) and cobalt-catalyzed *Z*-selective isomerization by Hilt *et al.* (bottom).

As already mentioned, the specialty of our method is that selectively one 1,3-hydride shift occurs in the isomerization process. This can be explained that diphenylphosphine, the co-ligand and isomerization promoter, takes part in the isomerization process, transferring the hydrogen atom directly to the substrate. This could be verified by deuterium labeling experiments. As a result, Hilt *et al*. proposed the mechanism depicted in Scheme 16 for the transformation.[32,33]

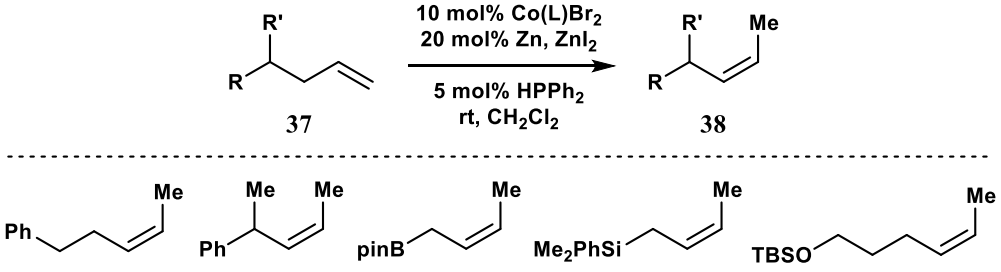
The hydrogen atom is reversibly transferred to the terminal position of the alkene from the $HPPh_2$ co-ligand coordinating to the active Co(I)-species **XV**. *β*-Hydride elimination of one of the allylic hydrides generates cobalt hydride **XVII**, which releases the *Z*-configured alkene. The active catalyst species has a higher affinity to the terminal alkene. A reinsertion of the 2-alkene *Z*-**36** is suppressed this way.[32]



Scheme 16: Proposed mechanistic pathway for the diphenylphosphine-assisted isomerization by Hilt.[32]

The reaction must be quenched at the point where a further conversion lowers the excess of the *Z*-configured product **36**, otherwise thermodynamic factors have to be taken into consideration, since the amount of *E*-isomer of **36** increased.

During her studies on the *Z*-selective isomerization, Anastasia Schmidt found a broad spectrum of α-alkenes **37** suitable for the reaction. Best results were obtained by varying the ligand and reaction time for each substrate guaranteeing optimal conversion of the starting material and excess of the *Z*-configured product.[32]



	39	40	41	22	14
ligand L	bdpp	bdpp	bdpp	bdpp	dpppBuEt
yield (*Z*/*E*)	92% (86:14)	84% (92:8)	96% (96:4)	91% (81:19)	95% (86:14)
remaining s.m.	10%	17%	3%	-	4%
other isomers	<1%	<1%	3%	<1%	<1%

Scheme 17: Selected substrates of Hilt's cobalt-catalyzed *Z*-selective isomerization.

Several functional groups were well-tolerated by the catalyst, such as aliphatic and branched alkyl chains, ethers, ketones and even a protic hydroxyl group as well as heteroatom-containing functional groups like silane **22**, silyl ether **14** or boronic ester **41**. On the downside, bulky groups and those with inherent coordinating abilities lead to inhibition of the catalyst. No conversion could be detected for the substrates shown in Figure 1.[33]

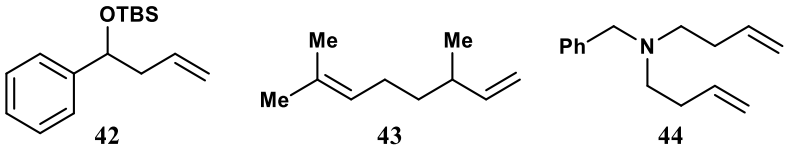


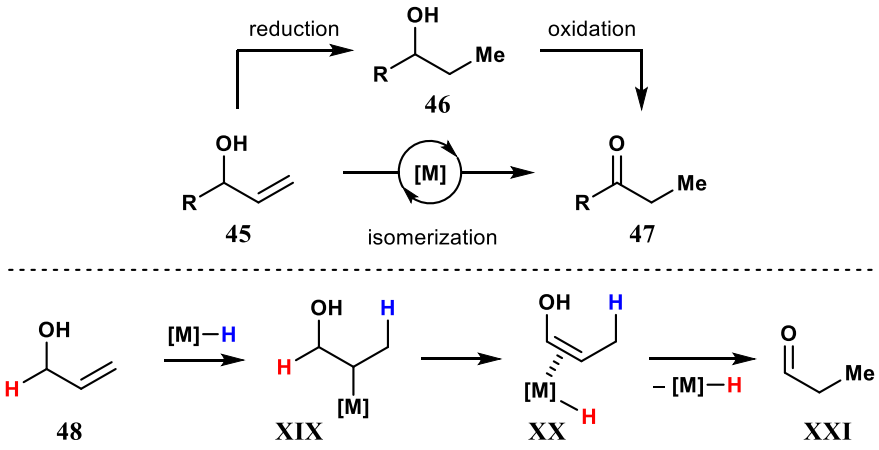
Figure 1: Substrates which do not work.

Especially amines like **44** and amides, not suitable for our group's cobalt-catalyzed isomerization, are of special interest, due to their high applicability in relevant follow-up reactions. Catalytic systems containing first-row transition metals other than cobalt can be found in the literature. Especially nickel and iron catalysts are able to induce the double bond transposition in *O*- and *N*-allyl systems.

1.1.3 Isomerization of O- and N-Allyl Compounds

The second category of olefinic substrates are the ones with an adjacent functional group, so-called "2-point binding substrates", which can coordinate to the catalyst and exert a direct influence on the catalyst's reactivity and selectivity.[14] Many 1,2-isomerizations of terminal alkenes are described for substrates substituted in the allylic position in which the chain walking is limited to one position. The allylic substituent (typically an ether, ester, or amide group) acts as π-acceptor and stabilizes the vinylic position, due to the conjugation of the double bond.[34] Moreover, allylic alcohols or ethers can serve as latent enol(ether) synthons.[35]

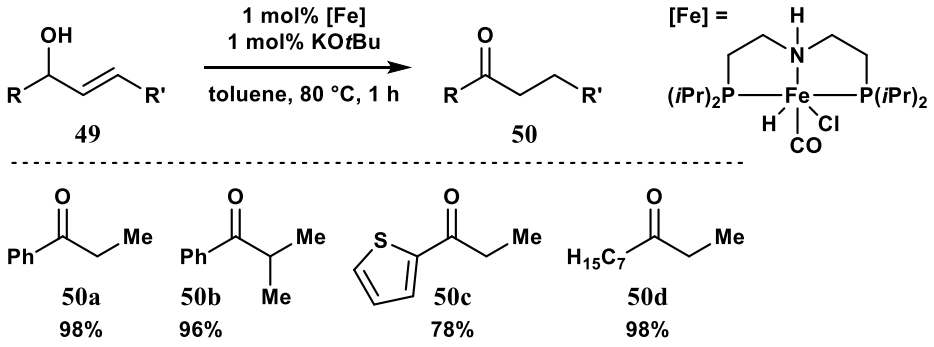
The double bond migration is a good alternative to the 2-step synthetic sequence of double bond reduction and alcohol oxidation (**45** → **46** → **47** in Scheme 18). In the last years, the catalyst development has given rise to efficient methods including enantioselective variants mainly catalyzed by precious transition metals, such as ruthenium, rhodium, or iridium.[36]



Scheme 18: Mechanism of the isomerization of allylic alcohols. [M]: typically Ru, Rh or Ir catalyst.

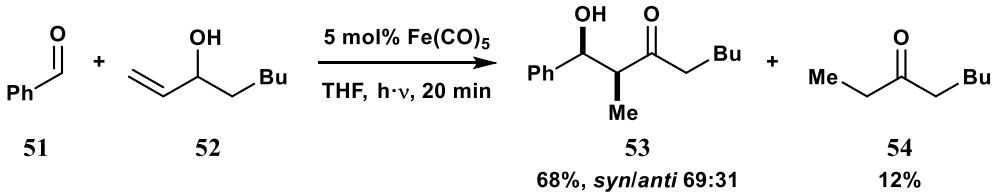
With focus on selected examples about first-row transition metal catalysis, Goetz *et al*. evaluated the potential of [$HCo(CO)_4$] serving for the isomerization of allylic alcohols during their investigations on olefin hydroformylation.[37] Furthermore, iron carbonyl complexes and nickel hydrides bear the potential of enolate formation by double bond transposition.[38]

A recent article by de Vries *et al*. describes the iron-catalyzed isomerization of allylic alcohol **49** to saturated ketone **50** (Scheme 19).[39]



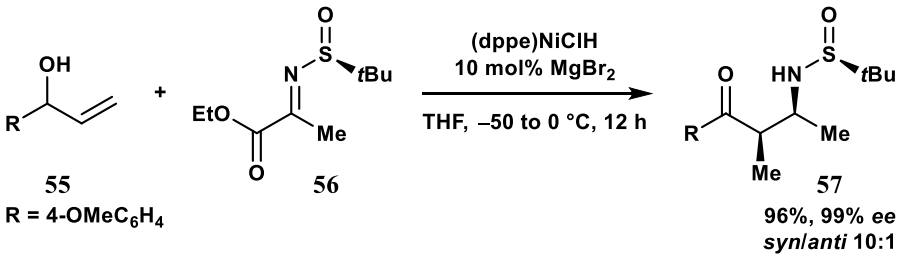
Scheme 19: Iron-catalyzed isomerization of substituted allylic alcohols by de Vries.

The isomerization of allylic alcohols is also applicable in one-pot sequences which are of special interest for my own work. One of the first examples shown in Scheme 20 was reported by Grée who used iron carbonyl catalysts for a moderately diastereoselective tandem isomerization/aldol reaction of benzaldehyde (**51**) and allylic alcohol **52**.[40]



Scheme 20: Iron-catalyzed one-pot isomerization/aldol-reaction sequence.

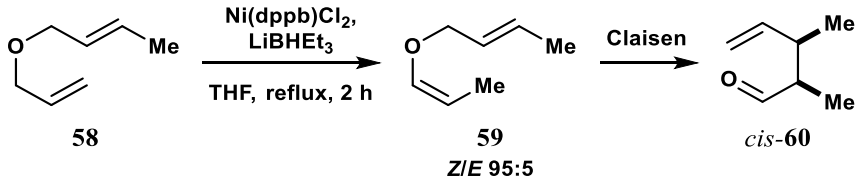
Furthermore, they presented a nickel pre-catalyst which was activated with a Grignard reagent and applied for a dia- and enantioselective isomerization/Mannich-type reaction sequence.[41]



Scheme 21: Nickel-catalyzed asymmetric one-pot isomerization/Mannich reaction sequence.

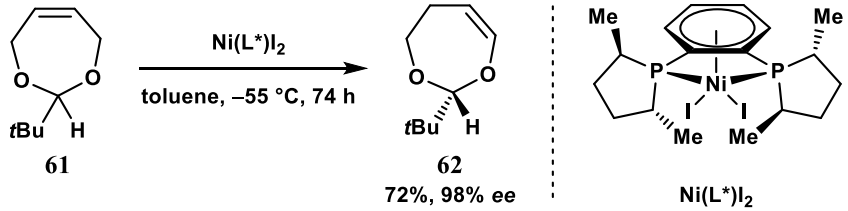
Frauenrath used $LiBHEt_3$ as reducing agent and hydride donor for his nickel precursor $Ni(dppb)Cl_2$ (dppb = bis(diphenylphosphino)butane) to achieve the isomerization of diallylic

ethers **58** followed by a Claisen rearrangement of enolether **59** to the resulting γ,δ-unsaturated aldehyde **60**. The method provides an excellent *Z*/*E* ratio of 95:5 and is shown in Scheme 22. It is restricted to allylic ethers, though, in which the transposition of the double bond is limited to a single 1,3-hydride shift.[13]



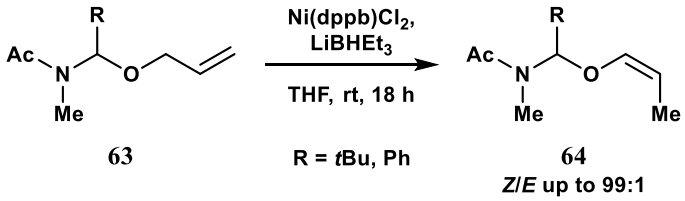
Scheme 22: *Z*-Selective isomerization of allyl ethers and subsequent Claisen rearrangement.

Frauenrath's modified catalyst system with the Me-DuPHOS ligand (L* in Scheme 23) could be further applied for an elegant kinetic resolution (KR) of acetal **61** *via* desymmetrization giving enantiomeric excesses (*ee*s) up to 98%.[42]



Scheme 23: KR by desymmetrization with a chiral nickel catalyst by Frauenrath.

Additionally, Frauenrath used his Ni(dppb)Cl_2/LiBHEt_3 catalyst systems for the isomerization of *N*-allyl acetals of type **63** obtaining excellent *Z*-selectivities up to 99:1.[42]



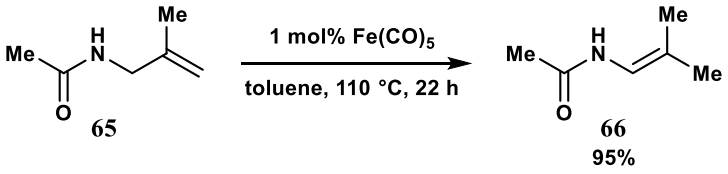
Scheme 24: Isomerization of *N*-allyl acetals by Frauenrath.

For the isomerization of *N*-allylic systems to enamides and enamines several transition metal catalysts are described in the literature.[18,43–46]

The Tagasako menthol process is a noteworthy industrial process illustrating the usefulness of a rhodium-catalyzed stereoconvergent isomerization to an enantiomerically enriched enamine (cf. chapter 1.2.1).

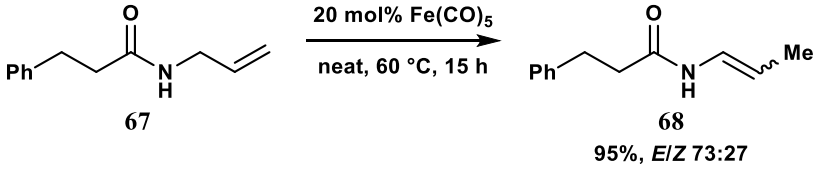
In case of first-row transition metals, there are several approaches to obtain enamides *via* isomerization of the corresponding allylic compounds. Starting with iron, Stille reported the

isomerization of substituted *N*-allyl amide **65** obtaining enamide **66** in good yield (95%), but poor selectivity (Scheme 25).[47]



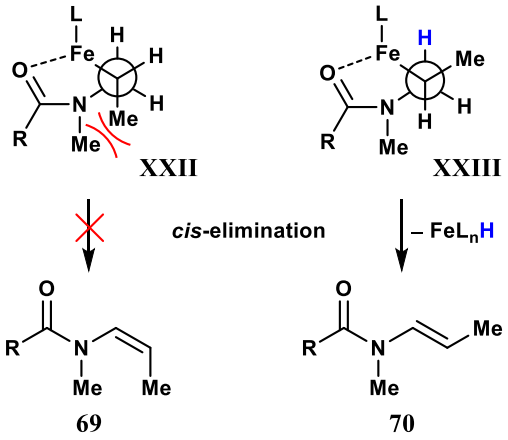
Scheme 25: Initial isomerization of *N*-allylic amides with iron carbonyl complexes.

20 years later, Hesse *et al*. used $Fe(CO)_5$ for a broader substrate scope and obtain *E*/*Z*-mixtures of the corresponding enamide **68** under neat conditions.[48]



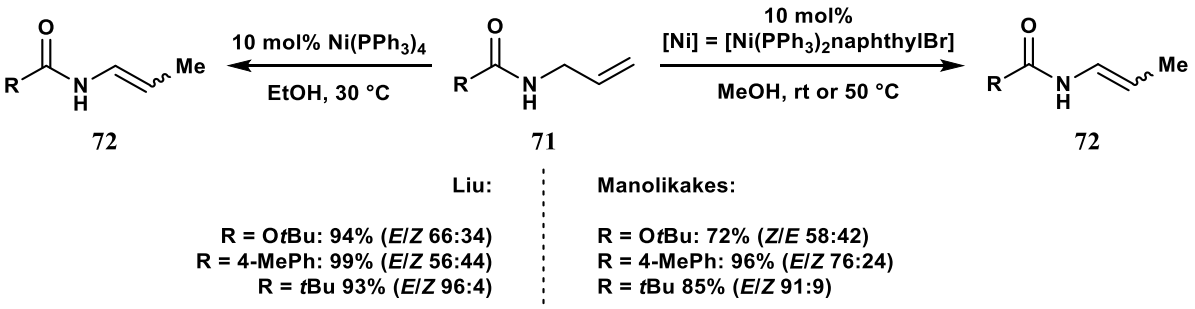
Scheme 26: Isomerization of *N*-allylic amides by Hesse.

As depicted in Scheme 27, they proposed the *E*-isomer being formed by coordination of the carbonyl moiety to the iron center (**XXIII**) and subsequent *cis*-elimination. Due to steric demand in intermediate complex **XXII** an elimination to the corresponding *Z*-isomer **69** is hindered.[48] They further describe long distance migration for their catalyst at somewhat higher temperatures (neat, 120 °C) to obtain enamides in a moderate *Z*/*E* ratio of 1:2 up to 1:3.[49]



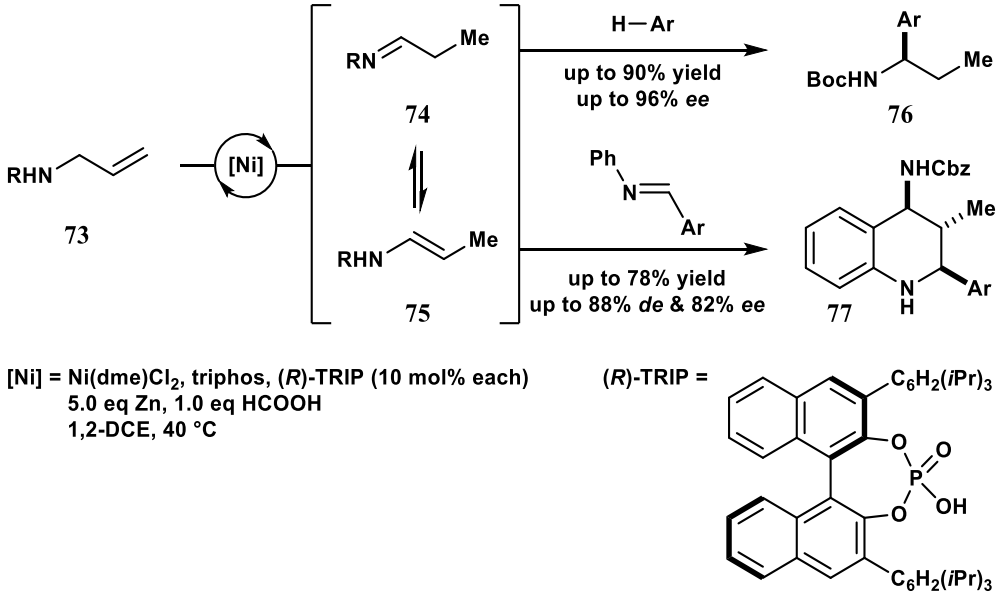
Scheme 27: Proposed mechanistic pathway for the iron-catalyzed isomerization of *N*-allyl amides explaining the stereochemical outcome.

For the nickel-catalyzed isomerization of *N*-allyl amides and carbamates **71** there are two methods described by Manolikakes[50] as well as Liu.[51] Both authors described the high reactivity of their catalyst systems giving mainly *E*-configured enamides or mixtures of *E*/*Z*-isomers in good yield. Scheme 28 depicts a comparison of both methods.



Scheme 28: Comparison of the isomerization of *N*-allylic amides and carbamates by Liu and Manolikakes.

A mechanistically divergent reaction sequence combining a nickel-catalyzed isomerization of *N*-allyl carbamates of type **73** with a subsequent enantioselective double bond functionalization could be achieved by the Moran group in 2016 and is shown in Scheme 29. The *in situ* generated imines or enecarbamates gave opposingly functionalized products. Formal α-functionalization of imine **74** provided α-arylamine **76** upon enantioselective Friedel-Crafts reaction, whereas the β-functionalization was achieved in an enantioselective Povarov cycloaddition to **77**.[52]

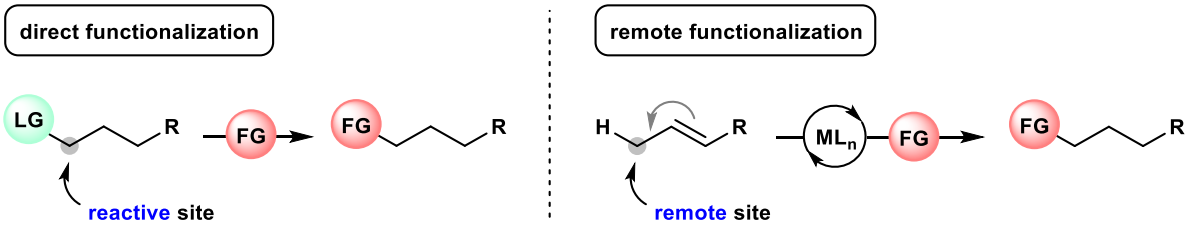


Scheme 29: Mechanistically divergent nickel-catalyzed isomerization/functionalization sequence by Moran triphos = (bis(diphenylphosphinoethyl)phenylphosphine, 1,2-DCE = 1,2-dichloroethane, dme = dimethoxy-ethane, Boc = *tert*-butoxy carbamate, Cbz = Carboxybenzyl).

The previous chapters described a targeted isomerization to achieve the double bond migration over exactly one position. Especially in allylic systems, multiple double bond migration is not possible. Chain walking of a metal hydride is a common phenomenon in substrates without adjacent functional group.

1.2 Remote Functionalization Through Double Bond Isomerization

As explained before, a double bond migration is not always limited to one position. Most of the mechanisms proceed *via* metal hydride species allowing multiple 1,3-hydride shifts along an aliphatic carbon chain through chain walking.[53] A recent example is Grotjahn's "alkene zipper" ruthenium catalyst, which is able to let the double bond "walk" 30 positions through an aliphatic chain.[54] Chain walking brings new possibilities to direct a follow-up reaction to a desired location in the molecule. A double bond transposition can be further seen as a remote functionalization leading to a selective reaction at a different position, the remote site.[8] Scheme 30 illustrates the concept of remote functionalization in comparison with the direct transformation of a molecule's most reactive site.

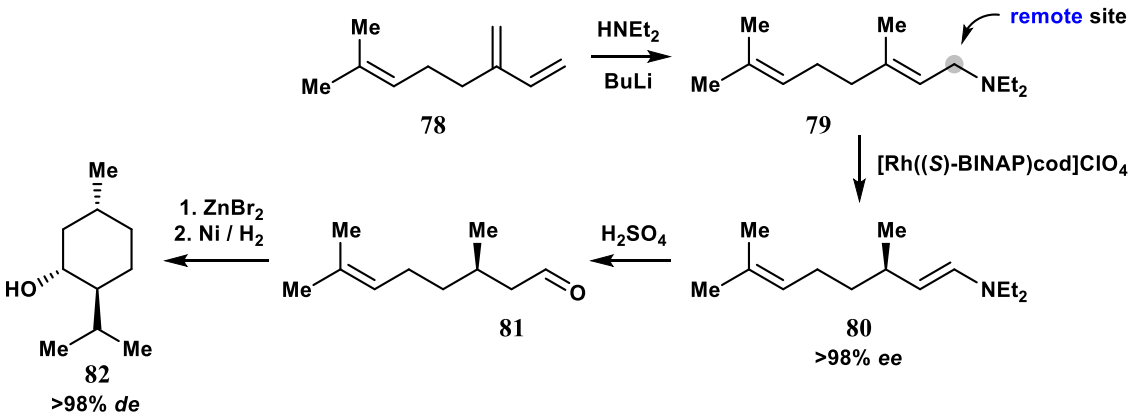


Scheme 30: Direct versus remote functionalization (LG = leaving group, FG = functional group).[11]

Taking advantage of a double bond's reactivity to generate another reactive site in a molecule is an ongoing challenge,[8] especially in academic and industrial research.

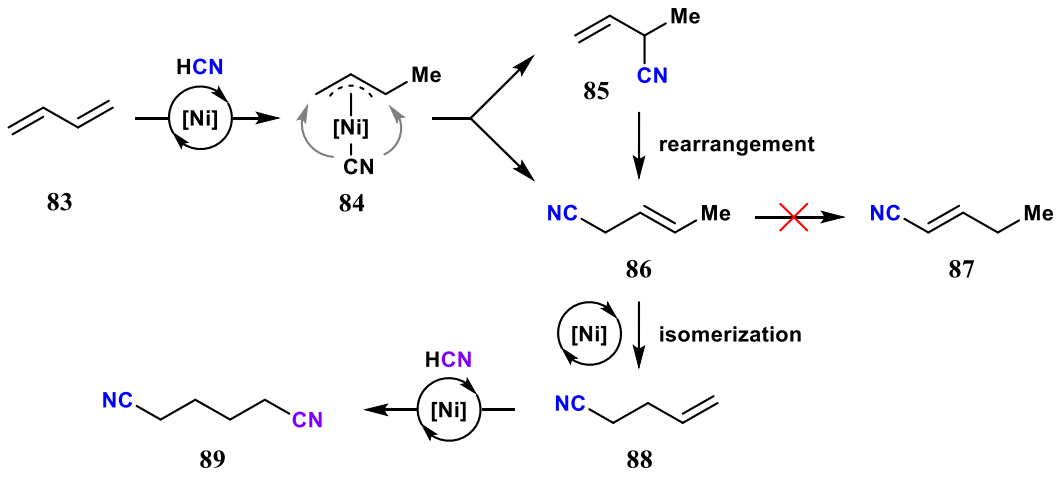
1.2.1 Relevance of Remote Functionalization for Chemical Industry

The transition metal-catalyzed olefin isomerization is of great value for industrial processes, since the double bond acts as popular group for further functionalizations. An asymmetric isomerization is used as key step in the Tagasako menthol process from myrcene (**78**) in which a chiral rhodium/(*S*)-BINAP catalyst established its first industrial usage. Scheme 31 illustrates the enantioselective isomerization of allylic amine **79** to the resulting enamine **80** in greater than 98% enantiomeric excess (*ee*). Subsequent functionalization allows the conversion of **80** to aldehyde **81** with final Lewis acid-assisted cyclization to (–)-menthol (**82**) in greater than 98% diastereomeric excess (*de*).[55,56]



Scheme 31: Enantioselective isomerization as key step in the Tagasako menthol process (BINAP = 2,2′-bis(diphenylphosphino)-1,1′-binaphthyl, cod = cycloocta-1,4-diene).

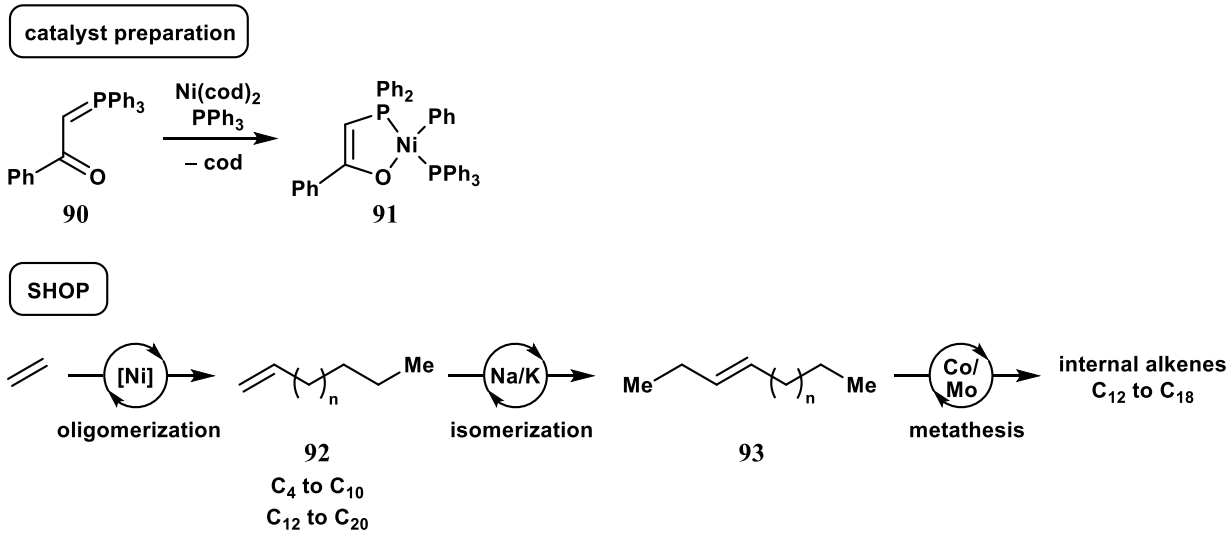
Especially tandem reactions are typical methods for the preparation of fine chemicals from petrochemicals. The DuPont adiponitrile process in Scheme 32 is a major success for industrial homogeneous catalysis involving a nickel(0)tetrakis(phosphite) catalyst for the three-step industrial synthesis of adiponitrile from 1,3-butadiene (**83**). The catalyst reacts with **83** in the presence of HCN and a Lewis acid to afford two mononitrile isomers **85** and **86**. **85** undergoes a skeletal rearrangement providing the desired linear product, crotylnitrile **86**.[57,58]



Scheme 32: DuPont adiponitrile process (simplified).

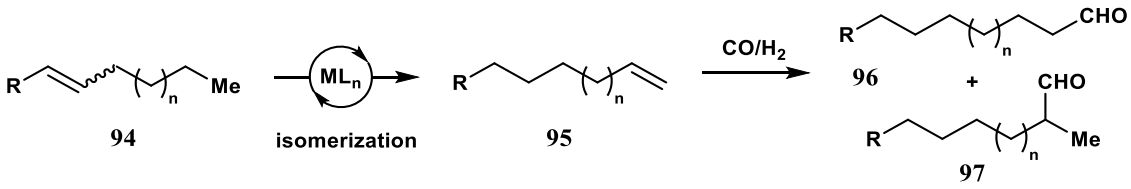
The subsequent nickel-catalyzed isomerization of crotylnitrile (**86**) is the crucial key step for formation of adiponitrile (**89**) by an *anti*-Markownikow hydrocyanation. Surprisingly, a kinetic preference of **86** compared to the thermodynamically favored vinylnitrile **87** occurs.[58]

Another remarkable industrial process is the Shell Higher Olefin Process (SHOP) comprising an oligomerization/isomerization/cross-metathesis sequence for the synthesis of fatty alcohols for detergents and surfactants. The homogeneous nickel phosphine complex **91** is used for the preparation of terminal alkenes of preferred length by ethylene oligomerization.[56,59]



Scheme 33: Shell Higher Olefin Process (SHOP) for the preparation of long-chain alcohols.[56]

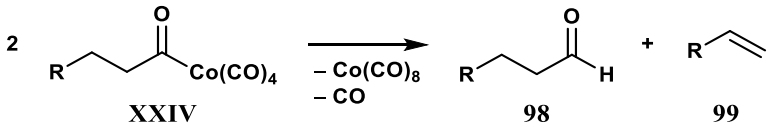
From all known examples of remote functionalization induced by transitions metals, the most common application with relevance in chemical industry is the isomerization/hydroformylation sequence convergently producing one defined product out of an isomeric mixture of the unsaturated starting material **94**. The treatment of an olefin **95** with syngas, a mixture of CO and H_2, leads to the formation of versatile carbonyl compounds **96**/**97** as Scheme 34 illustrates.[8,60] The formation of linear aldehydes **96** is only reached when the isomerization occurs faster than the CO insertion.



Scheme 34: Schematic tandem isomerization/hydroformylation process.

The observation that ethylene, H_2, and CO were converted into propanal in the cobalt-catalyzed Fischer-Tropsch reaction, marked the beginning of hydroformylation catalysis.[61] Since then, the cobalt-catalyzed isomerization/hydroformylation process has a high industrial relevance and is numerously presented in literature.[60,62]

The isomerization reaction proceeds *via* chain walking of the metal hydride to give all possible isomers. The observation, that a general tendency for the formation of linear aldehydes is independent of the starting molecule, indicates a strong kinetic preference for the irreversible formation of a (*n*-alkyl)acyl-cobalt intermediate **XXIV** in the hydroformylation step.[63]

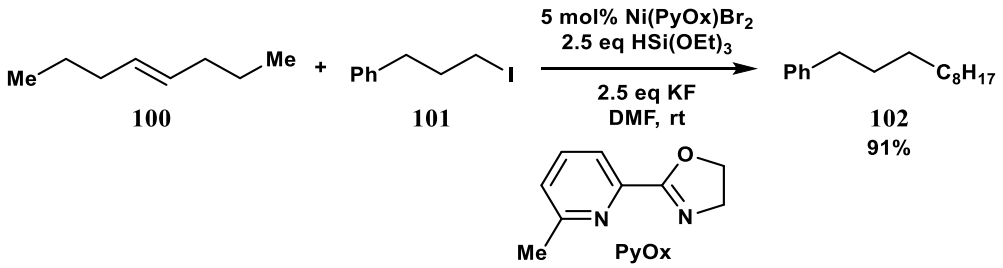


Scheme 35: Disproportionation of a (*n*-alkyl)acyl-Co species.

Large-scale technical processes usually operate at high temperatures (120−175 °C) and high CO pressure (270−300 bar) providing 60−70% *n*-aldehydes. A modification of the catalyst with bulky phosphine ligands generally increases thermal stability and favors the formation of linear aldehydes. The regioselectivity can be increased to 75−90%. As a drawback, alcohols are preferentially formed due to the enhanced hydrogenation activities of $[HCo(CO)_3PR_3]$.[58] An isomerization and subsequent hydrogenation is also known for nickel-containing catalyst systems.[64] Besides hydroformylation, there are also other reactions suitable for remote functionalization in a one-pot fashion. They will be presented in the following chapter.

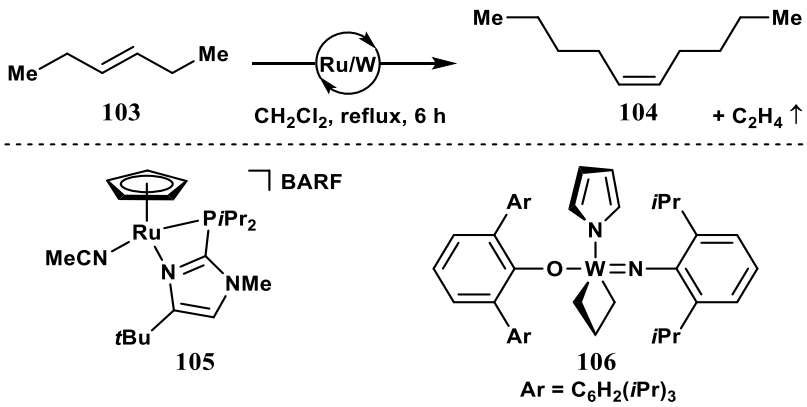
1.2.2 One-pot Isomerization Sequences

Nickel-catalyzed double bond migration is nowadays used as attractive remote strategy to form bonds between otherwise unactivated carbon centers.[65,66] Zhu and co-workers described several approaches using dual nickel catalysis for isomerization and a subsequent cross-coupling reaction to form C–C bonds between sp^2/sp^3 and sp^3/sp^3-hybridized carbon atoms.[65,67,68] This year, the Zhu group presented a nickel hydride-species, formed upon reduction of the Ni(II)-precursor with triethoxysilane, catalyzing the isomerization of unrefined olefin mixtures **100** and the subsequent remote hydroalkylation for the construction of $C(sp^3)–C(sp^3)$ bonds.[67] The reaction is illustrated in Scheme 36.



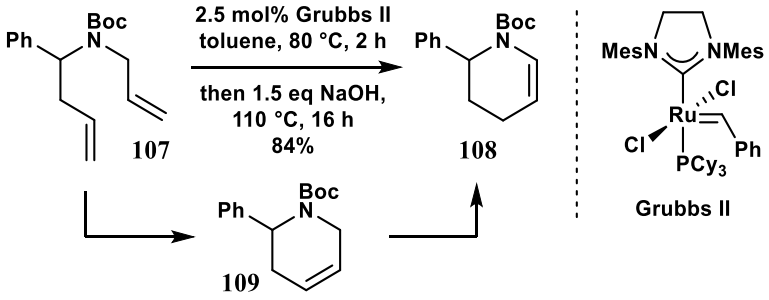
Scheme 36: Remote reductive hydroalkylation of terminal alkenes (DMF = *N*,*N*-dimethylformamide).

Similar to the SHOP, Grotjahn and Schrock published an elegant isomerization/cross-metathesis sequence catalyzed by a co-catalyst system comprising Grotjahn's "alkene-zipper" (ruthenium catalyst **105**) and tungsten catalyst **106**, which had a strong preference for terminal olefins to give *Z*-configured internal alkenes as **104** in olefin metathesis (Scheme 37).[69]



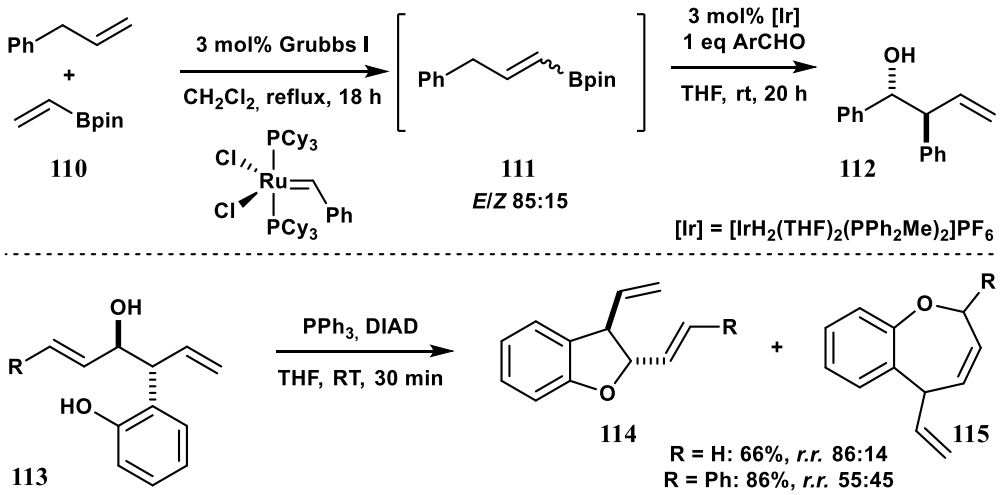
Scheme 37: Isomerization/cross-metathesis sequence with "alkene-zipper"/tungsten co-catalysis.

An application of the Grubbs II catalyst for ring closing metathesis (RCM) and subsequent isomerization of the corresponding cyclic allyl urethane **109** was described by Schmidt (Scheme 38).[70] A similar approach for the one-pot synthesis of indoles by an isomerization/enamide-ene metathesis reaction sequence was reported by Shuto in 2011.[71]



Scheme 38: Tandem RCM/isomerization sequence by Schmidt.

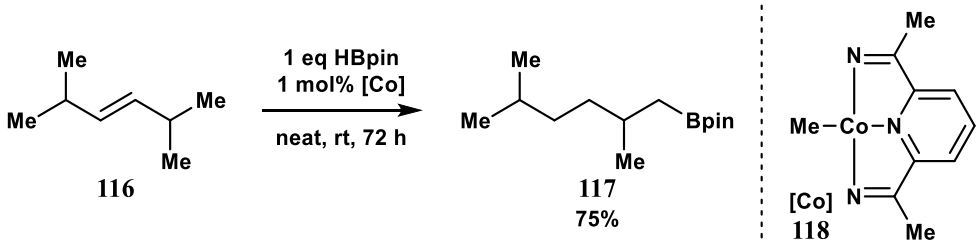
The Carboni group upgraded the isomerization/metathesis sequence with a subsequent allylboration step after metathesis of vinyl boronic ester **110** and allylbenzene (**17**) with Grubbs I catalyst and iridium-catalyzed *E*-selective isomerization of the resulting vinyl boronic ester **111** giving rise to *anti*-configured homoallylic alcohol **112** (Scheme 39, top), and bioactive neolignane structures **114**/**115** (Scheme 39, bottom).[72]



Scheme 39: Tandem isomerization/cross-metathesis/allylboration reaction by Carboni (*r.r.* = regioisomeric ratio).

1.2.3 Hydroboration/Isomerization/Allylboration Sequences

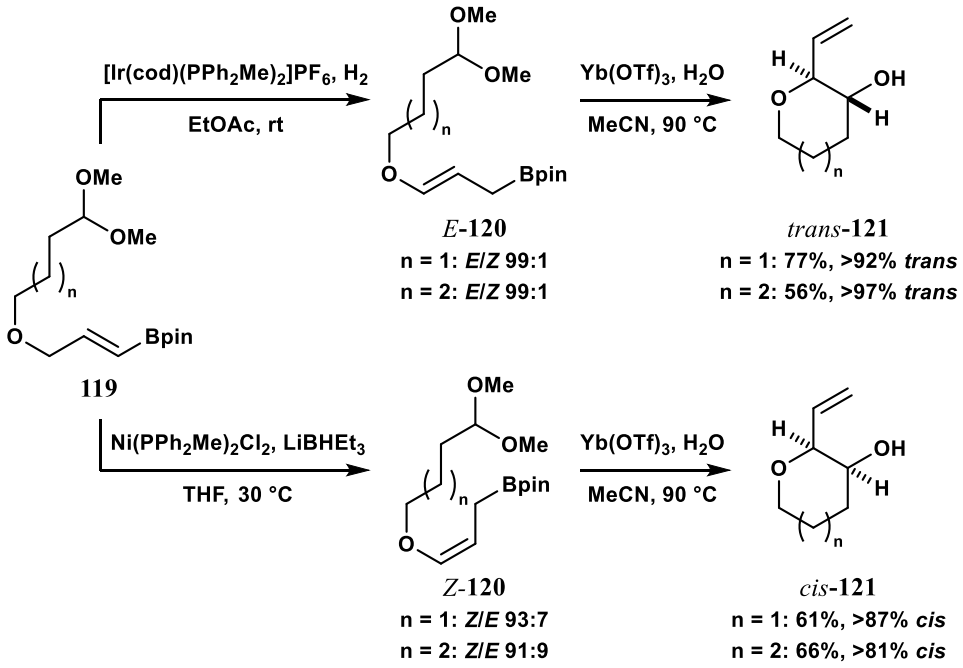
The diverse chemistry of organoboron compounds can also be exploited in combination with an isomerization reaction. Chirik *et al.* described an aryl-substituted bis(imino)pyridine cobalt methyl complex (**118** in Scheme 40) for alkene hydroboration. For internal olefins such as **116**, an isomerization to the terminal position was observed first, providing a selective hydroboration of the remote C−H bond.[73]



Scheme 40: Cobalt-catalyzed isomerization/hydroboration sequence by Chirik *et al*.

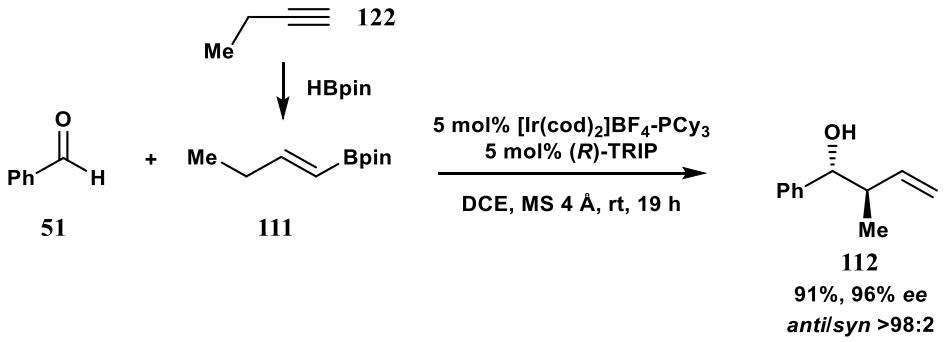
Since vinylboronic acids are easily prepared from terminal alkynes through hydroboration, it is necessary to isomerize the double bond to the allylic position enabling an allylboration reaction with carbonyl moieties. A modification of Carboni's iridium catalyst (cf. Scheme 39) was applied by Miyaura for the isomerization of the vinylic boronic ester **119** to enolether *E*-**120** and subsequent intramolecular allylboration to give *trans*-tetrahydropyranols **121** and tetrahydrooxepanols in good diastereoselectivity of up to 97% (Scheme 41, top). As reported earlier, nickel is known for the *Z*-selective isomerization of allyl ethers to their corresponding enolethers.[13] Therefore, the *cis*-configured cyclic ethers **121** could be obtained by a *Z*-selective isomerization with a catalyst system comprising $Ni(PPh_2Me)_2Cl_2/LiBHEt_3$ (cf. Scheme 41,

bottom) and subsequent allylboration. Either way, deprotection of the acetal group was achieved by addition of the Lewis acid $Yb(OTf)_3$.[74]



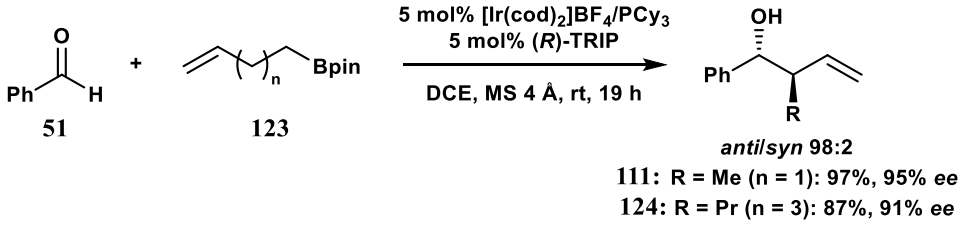
Scheme 41: Tandem hydroboration/isomerization/allylboration sequence by Miyaura.

For the *E*-selective isomerization of vinyl boronic esters another iridium catalyst was described by Murakami *et al.* in 2013. Starting from the desired terminal alkyne **122** they could get access to *anti*-configured homoallylic alcohol **112** in a hydroboration/isomerization/allylboration sequence. The final allylboration step could be achieved enantioselectively by utilization of the chiral phosphoric acid (*R*)-TRIP leading to excellent enantiomeric excesses of up to 96%.[75]



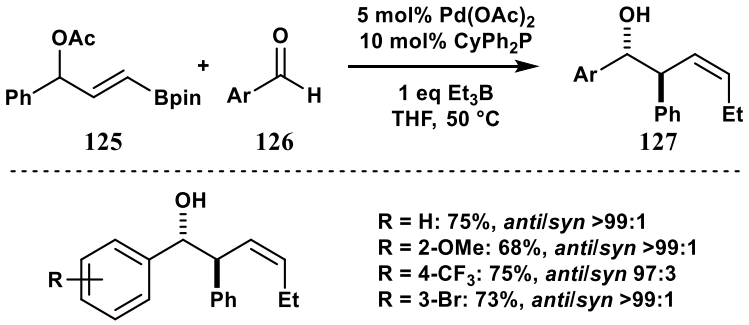
Scheme 42: Enantioselective hydroboration/isomerization/allylboration sequence by Murakami *et al.* ((*R*)-TRIP = (*R*)-3,3′-bis(2,4,6tri*iso*propyl-phenyl)-1,1′-binaphthyl-2,2′-diyl hydrogenphosphate).

Further, the migration of the double bond could be accomplished in two different ways. Scheme 42 illustrates the transposition away from the functional group whereas Murakami also described an isomerization towards the boronic ester functionality of **123**.[75]



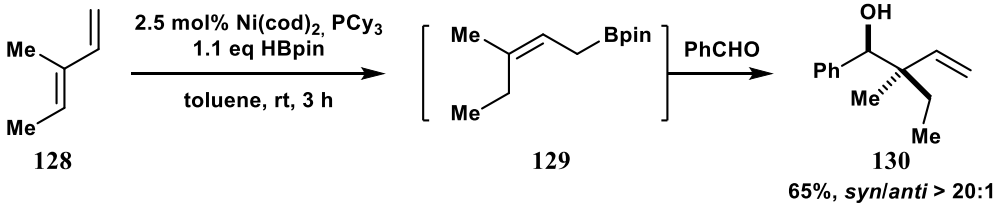
Scheme 43: Murakami's iridium-catalyzed isomerization towards the functional group.

Another three-component reaction was published by Horino and Abe in 2015. They used a palladium catalyst for the double bond transposition of allyl acetates **125** and subsequent *Z*-selective Suzuki cross-coupling of the resulting enol acetates (Scheme 44) and triethylborane.[76] In 2017, they described a similar reaction using aryl tin organyls as transmetalating agent.[77]



Scheme 44: Isomerization/cross-coupling sequence by Horino.

Concerning the hydroboration of 1,3-dienes, a nice example was published by Morken *et al*. They used a $Ni(cod)_2/PCy_3$ catalyst for a 1,4-hydroboration of 1,3-diene **128** and the subsequent allylboration of the resulting allylboronic ester **129** giving rise to *syn*-configured alcohol **130** with good diastereoselectivity *syn*/*anti* up to 20:1.[78]

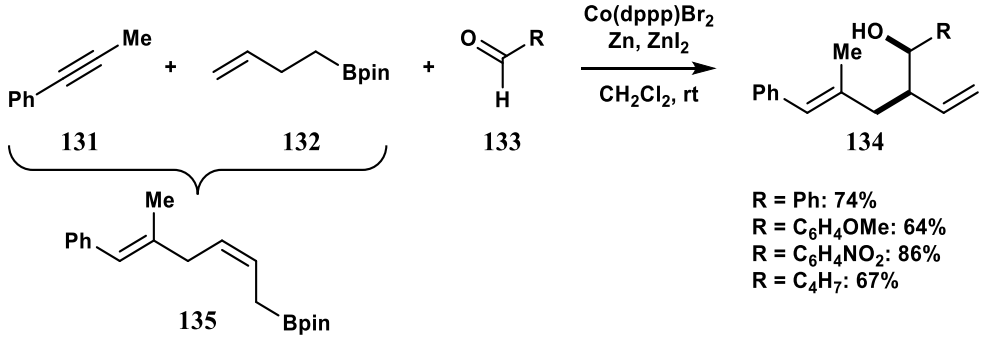


Scheme 45: Nickel-catalyzed 1,4-hydroboration of 1,3-dienes and subsequent allylboration.

As shown above, the allylboration acts as a powerful follow-up reaction, not only for hydroboration, metathesis or isomerization. The Hilt group has investigated the allylboration as subsequent process for cobalt-catalyzed transformations.

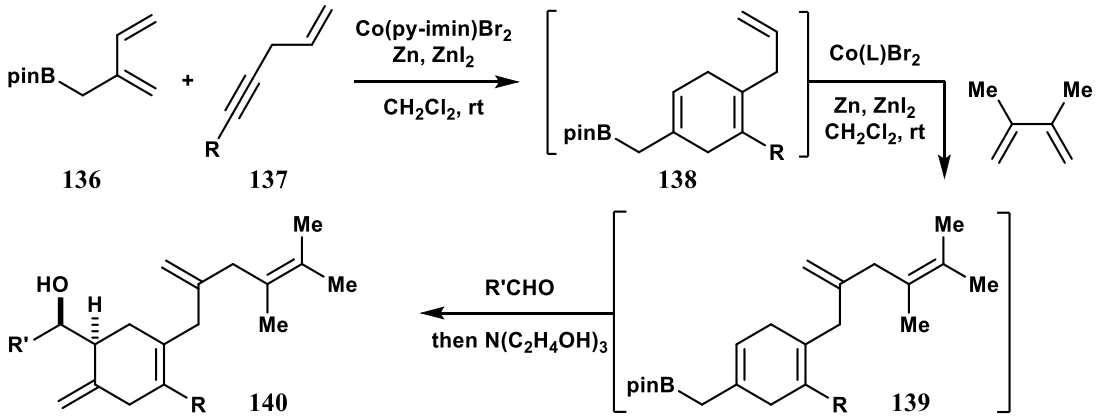
1.2.4 Allylboration Sequences in the Hilt Group

The Hilt group achieved various cobalt-catalyzed transformations, such as the hydrovinylation, Diels-Alder and Alder-ene reaction, in combination with an allylboration to get access to highly functionalized target molecules in good regioselectivity.[77,78] The cobalt-catalyzed Alder-ene reaction of homoallylboronic ester **132** was combined with an allylboration to the corresponding *syn*-configured homoallylic alcohols of type **134**. The first step of this multicomponent reaction is the formation of intermediate **135** with a *Z*-configured allylboronate moiety *via* Alder-ene reaction as shown in Scheme 46.[79]



Scheme 46: Three-component Alder-ene/allylboration process by Sušnik and Hilt.

In 2012, Erver and Hilt presented a four-component reaction of an allylboronic ester **136**, 1,4-enyne **137**, dimethylbut-1,3-diene and an aldehyde R'CHO with a Diels-Alder/hydrovinylation/allylboration sequence leading to *syn*-configured polyenol structures **140**.[80]



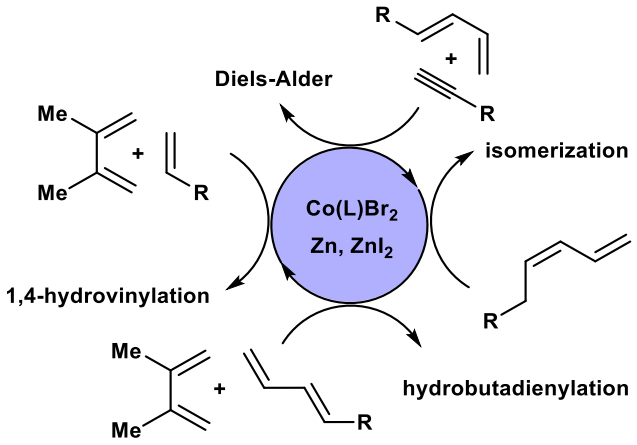
Scheme 47: Four-component reaction by Erver and Hilt.

The application of 1,3-dienes is not only limited to allylboration sequences. The following chapter will describe other applications of substrates with 1,3-diene subunit in the Hilt group and give a short overview of recent cobalt-catalyzed hydroacylation reactions.

1.3 Cobalt-Catalyzed Transformations of Terminal Alkenes and 1,3-Dienes

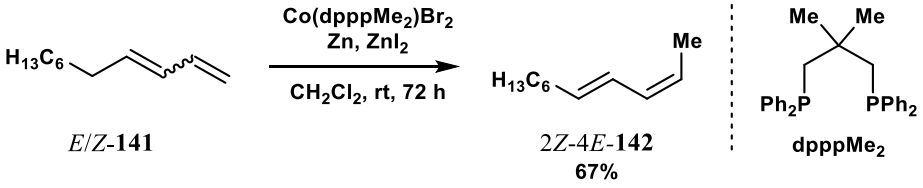
1.3.1 Cobalt-Catalyzed Isomerization and Hydrovinylation of 1,3-Dienes

Cobalt-catalyzed transformations of 1,3-dienes are a central research area in the Hilt group. The formation of the active Co(I)-species follows the pathway presented in Scheme 15 and can be transferred to all of our cobalt-catalyzed reactions, such as the Diels-Alder reaction,[81–85] the hydrovinylation,[86–88] hydrobutadienylation,[89,90] or the afore-mentioned isomerization of terminal alkenes[32] as well as 1,3-dienes.[91] Scheme 48 gives a brief overview.



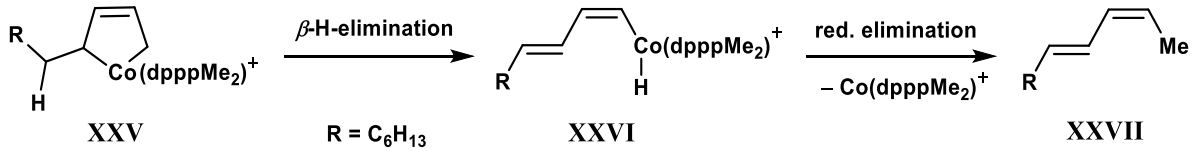
Scheme 48: Selected cobalt-catalyzed transformations of 1,3-dienes in the Hilt group.

An isomerization step is not only limited to a single double bond. In case of 1,3-dienes, a formal 1,5-hydride shift is also possible. In 2012, our group described a stereoconvergent isomerization of terminal 1,3-dienes leading to two different types of products depending on the ligand structure of the cobalt catalyst. The method could be successfully applied in the total synthesis of Urushiol.[92] Co(dpppMe$_2$)Br$_2$ isomerizes the terminal 1,3-diene **141** to the corresponding 2*Z*-4*E*-diene **142** as depicted in Scheme 49.[91]



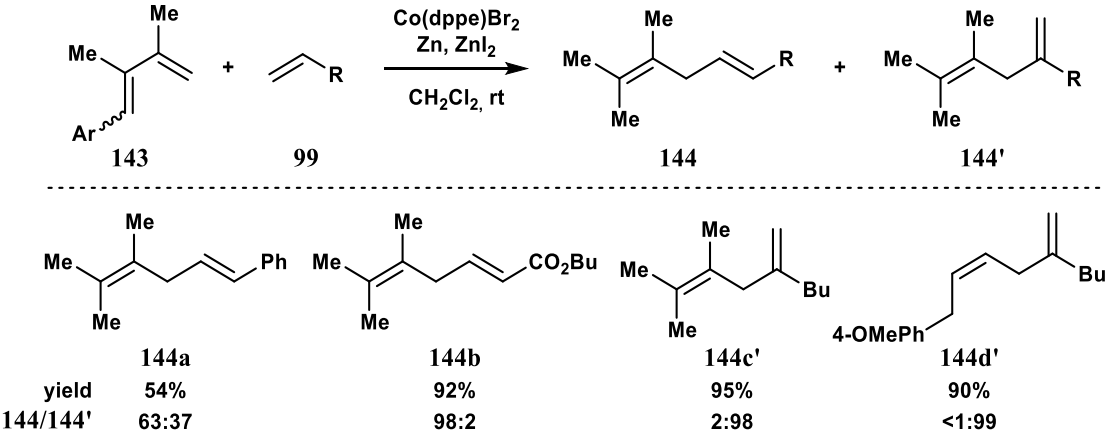
Scheme 49: Stereoconvergent cobalt-catalyzed isomerization of 1,3-dienes by Hilt.

The generation of products of type 2*Z*-4*E*-**142** is a formal 1,5-hydride shift, in which the *E*-configured double bond is formed due to the *syn*-selectivity of the *β*-hydride elimination step. The 2*Z*-double bond is intermediary predetermined by formation of the cobaltacyclopentene complex **XXV** with *β*-hydride-elimination and reductive elimination of **XXVI**.[91]



Scheme 50: Proposed mechanistic pathway for the formal 1,5-hydride shift.

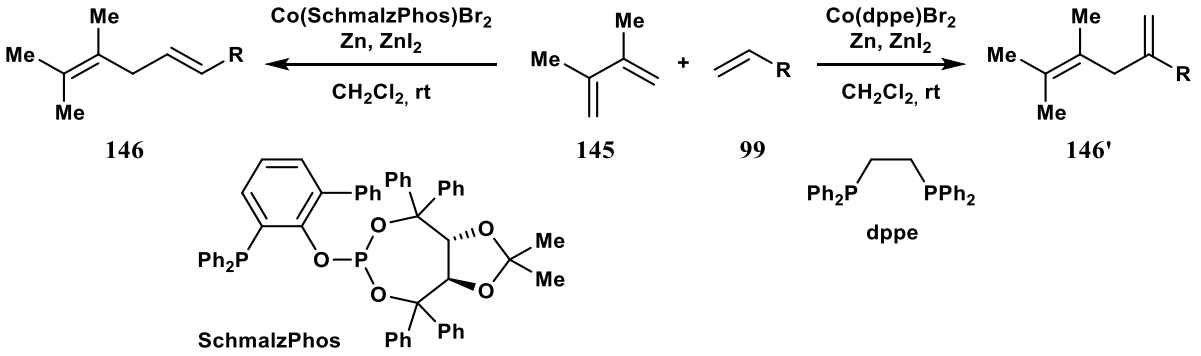
Another popular application of 1,3-dienes is the hydrovinylation reaction. In the RajanBabu[93] and the Hilt group several approaches concerning cobalt and nickel-catalyzed variants with different regioselectivities were developed.[87,94]



Scheme 51: Regioselectivity of the cobalt-catalyzed 1,4-hydrovinylation of 1,3-dienes with alkenes.

The 1,4-hydrovinylation, shown in Scheme 51, provided linear or branched products depending on the steric and electronic nature of the alkene. Non-conjugate alkenes predominantly formed the branched 1,4-diene **144'** with an *exo*-double bond whereas acrylates formed the linear product **144**. When styrene is used, only a moderate preference of the linear product with a **144a**/**144a'** ratio of 63:37 was observed. Unsymmetrical 1,3-dienes can give up to four regioisomers.[87,94]

The regioselectivity of the hydrovinylation could also be controlled by variation of the ligand. Utilization of the bulky SchmalzPhos ligand (see Scheme 52) allowed the formation of the linear product **146** with unactivated neutral alkenes **99** and 2,3-dimethylbuta-1,3-diene (DMB, **145**). In contrast, dppe as ligand would give the branched products of type **146'**. Limitation of the SchmalzPhos ligand was that only 2-substituted 1,3-dienes could be used, otherwise the alkene was not completely consumed.[95]



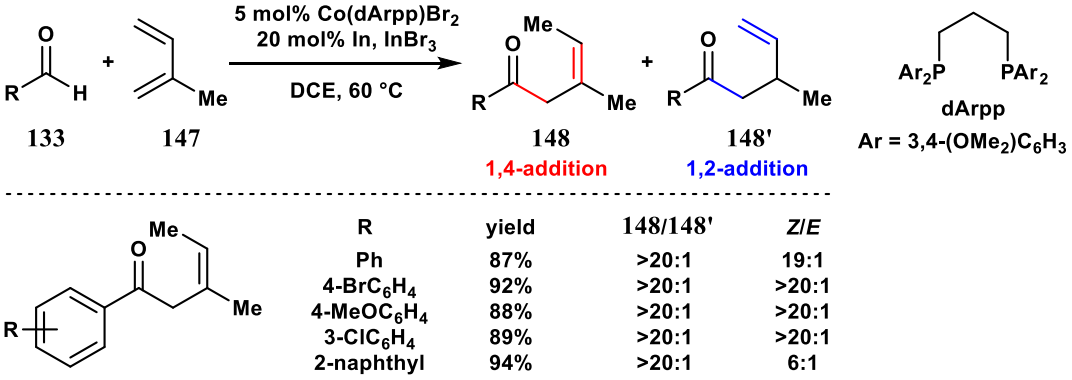
Scheme 52: Control of the regioselectivity by ligand variation.

Last year, our group developed a novel multi-component reaction comprising a regioselective cobalt-catalyzed hydrovinylation combined with a Wittig olefination of unsaturated phosphonium salts and 1,3-dienes for the synthesis on non-conjugated trienes with a well-defined double bond location and configuration.[96]

Instead of using an olefinic double bond in a hydrovinylation process, the application of a carbonyl moiety leads to a hydroacylation of 1,3-dienes.

1.3.2 Hydroacylation of Terminal Alkenes and 1,3-Dienes

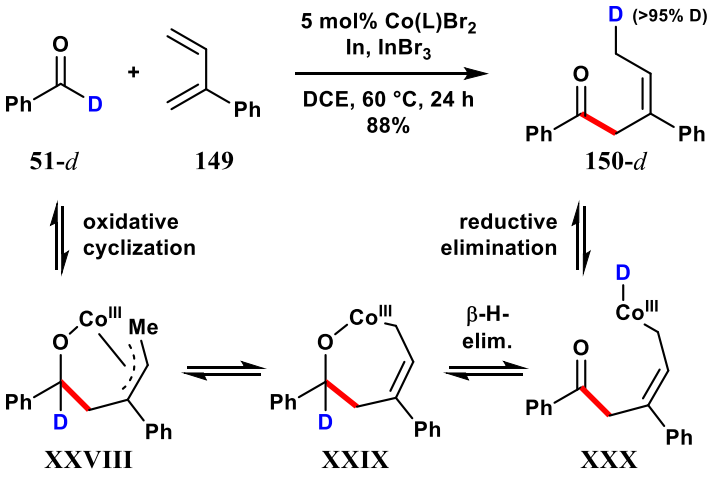
A hydroacylation is a formal alkene insertion into a formyl C-H-bond. The Dong group has established a cobalt-catalyzed intermolecular 1,4-hydroacylation leading to a new regioselectivity in the product with a **148**/**148'** ratio greater than 20:1.[97]



R	yield	148/148'	*Z*/*E*
Ph	87%	>20:1	19:1
4-BrC$_6$H$_4$	92%	>20:1	>20:1
4-MeOC$_6$H$_4$	88%	>20:1	>20:1
3-ClC$_6$H$_4$	89%	>20:1	>20:1
2-naphthyl	94%	>20:1	6:1

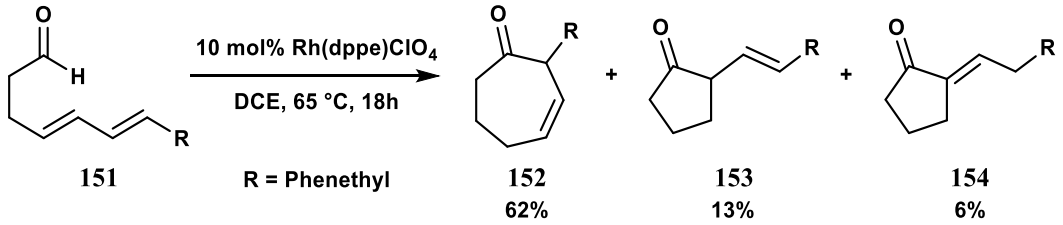
Scheme 53: Intermolecular hydroacylation by the Dong group.

They propose the mechanism illustrated Scheme 54. When the hydroacylation was performed with *deutero*-benzaldehyde (**51**-*d*), the deuterium atom was incorporated at position 4 of the diene **149** without any detectable deuterium at other positions. This result suggests that the hydroacylation with aromatic aldehydes proceeds through a 1,4-addition pathway with seven-membered cobaltacycle **XXIX**.[97]



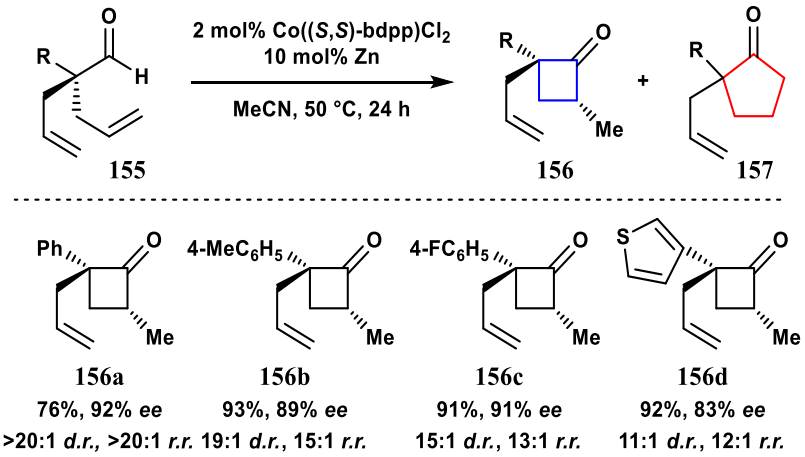
Scheme 54: Deuterium labeling for a mechanistic proposal of the 1,4-hydroacylation with 1,3-dienes.

An intramolecular hydroacylation of 1,3-dienes can be performed *via* rhodium catalysis and was described by Sato *et al*. in 2007. The reaction generated products with cyclohept-3-en-1-one structure (**152**) whereas the cyclization of the inner double bond to the five-membered ring substructures (**153** and **154**) was observed as side-reaction. Their mechanistic proposal proceeds through a π-allylrhodium intermediate, similar to Dong's cobalt species **XXIX** in Scheme 54.[98]



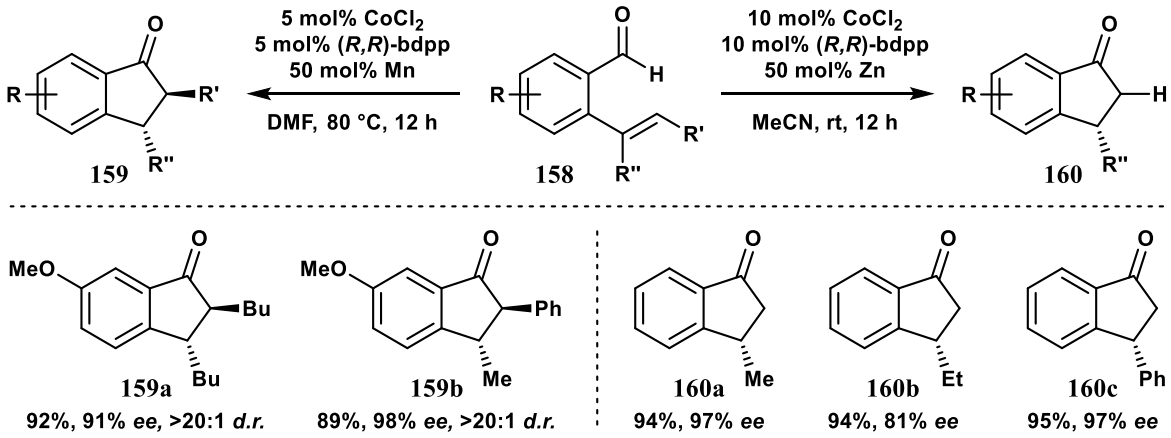
Scheme 55: Rh-catalyzed intramolecular hydroacylation of 1,3-dienes.

Dong *et al.* further described an intramolecular enantioconvergent hydroacylation of terminal olefins leading preferably to cyclobutanone moieties **156** with excellent diastereo-, regio- and enantiocontrol in a diastereomeric ratio (*d.r.*) up to >20:1 and enantiomeric excesses (*ee*) greater than 90%. The formation of five-membered rings of type **157** was not observed.[99] The reaction is illustrated in Scheme 56.



Scheme 56: Intramolecular hydroacylation for the formation of cyclobutanones (bdpp = pentane-2,4-diylbis-(biphenyl-λ^4-phosphane), *r.r.* = regioisomeric ratio).

Another enantioselective variant of cobalt-catalyzed intramolecular hydroacylations was described by Yoshikai *et al*. and shown in Scheme 57.[100,101]



Scheme 57: Enantioselective intramolecular hydroacylation of styrene derivatives.

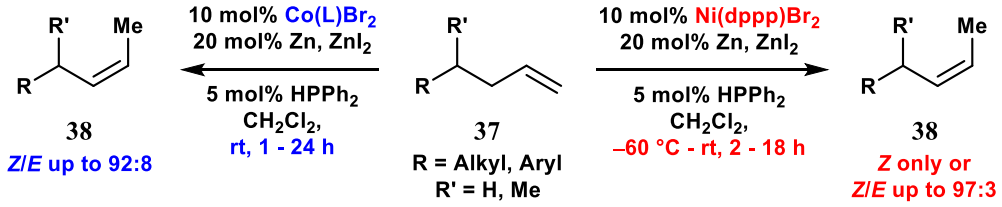
They used either mono- or disubstituted styrene derivatives **158** for the formation of up to two stereocenters in the products of type **159** or **160** with excellent enantiomeric excesses (*ee*) and diastereomeric ratios (*d.r.*) greater than 20:1 (Scheme 57).[100,101]

To the best of my knowledge, there is no cobalt-catalyzed intramolecular hydroacylation of 1,3-dienes described in literature, yet. The application of the Hilt catalyst system in a possible hydroacylation reaction would expand our research expertise concerning cobalt and nickel-catalyzed reactions for C–C-bond formation and migration processes.

2. Research Objective

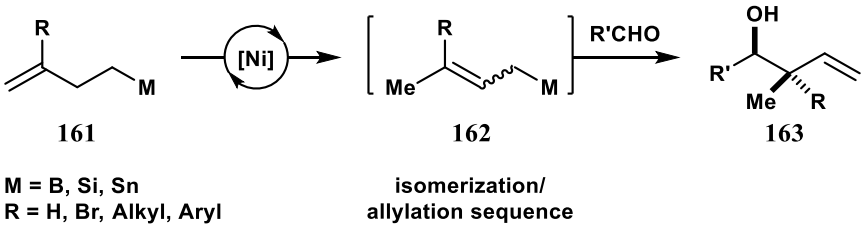
2.1 Scope, Application and Mechanism of the Nickel-Catalyzed *Z*-Selective Isomerization

In 2014, Anastasia Schmidt identified a cobalt catalyst system for the *Z*-selective monoisomerization of α-olefins **37** to 2-alkenes **38**. The use of diphenylphosphine had a significant impact concerning selectivity and reactivity.[32,33] During my Master thesis, the neighboring nickel catalyst showed even better *Z*-selectivity, an outstanding reactivity even at low temperatures, and a high functional group tolerance for the same transformation.[102]



Scheme 58: Comparison of the cobalt and nickel-catalyzed *Z*-selective isomerization of terminal alkenes.

In the course of this work, the substrate scope shall be investigated to get access to higher functionalized target molecules. The nickel-catalyzed isomerization should be applicable for 2-point binding substrates, such as *N*-allyl amides or carbamates. Suitable follow-up reactions, such as an allylation of carbonyl compounds R'CHO, can be performed as one-pot sequence to illustrate scope and possible limitations of the nickel catalyst.



Scheme 59: Proposed nickel-catalyzed isomerization/allylation sequence of homoallylic substrates.

The structure motif of conjugated and non-conjugated diene substructures can be found in pheromones. To demonstrate the applicability of the method in natural product synthesis, a cobalt and nickel-catalyzed isomerization of the corresponding 1,4- and 1,5-dienes as starting material is worth to be examined as an atom-economic alternative to conventional cross-coupling reactions or metathesis. The potential target structures are shown in Figure 2.

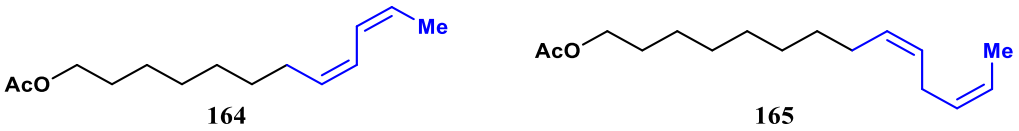


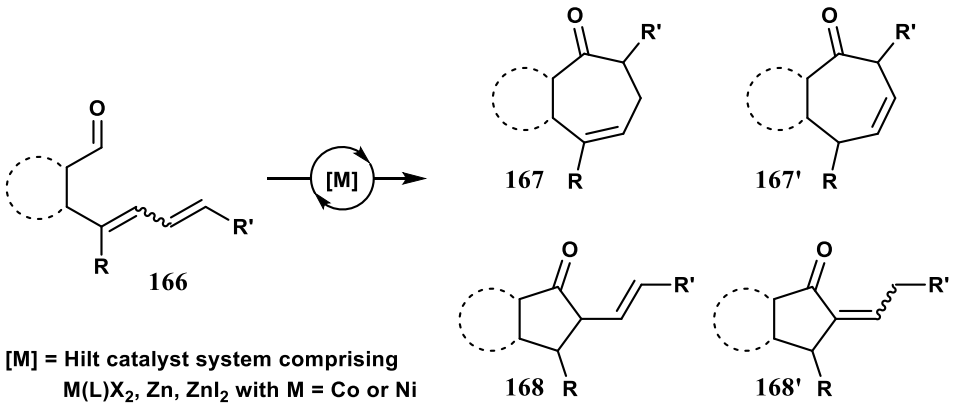
Figure 2: Pheromones with 2*Z*,4*Z*- and 2*Z*,5*Z*-diene substructure as target molecules.

The pivotal isomerization step would contain a threefold challenge: generation of high *Z*-selectivity in presence of another intern double bond without converting the diene substructure into a conjugate system (in case of the 1,5-diene).

A mechanistic investigation of the isomerization process is desired. The investigations shall give insight into the elementary steps of the reaction on the one hand and the source of the stereochemical outcome of the reaction for both, cobalt and nickel catalyst, on the other. EPR and CV measurements should give information about the oxidation state and ligand sphere of the active catalyst species, since NMR spectroscopy is not suitable for the detection of paramagnetic species. Theoretical investigations are targeted to reveal the mode of action of the crucial co-ligand diphenylphosphine and to propose a defined mechanistic pathway.

2.2 Cobalt-Catalyzed Hydroacylation of 1,3-Dienes

On the path for the development of new nickel and cobalt-catalyzed transformations of alkenes and 1,3-dienes, the hydroacylation of 1,3-dienes is still missing in the Hilt group's research expertise, which is mainly based on isomerization, cycloaddition, Alder-ene, Diels-Alder and hydrovinylation reactions (for an overview, see Scheme 48).[81–92] The proposed reaction, an intramolecular hydroacylation of diene **166**, is inspired by former work of the Dong group[97] and is shown in Scheme 60.



Scheme 60: Planned conjugate intramolecular hydroacylation of 1,3-dienes. Up to 4 regioisomers are possible.

Once the reaction conditions towards the desired intramolecular hydroacylation or cyclization have been optimized, the substrate scope shall be further explored. For initial investigations, the aldehyde function and 1,3-diene subunit should both be present within the starting material. Further, the translocation of the formyl hydrogen atom shall be revealed by deuterium labeling experiments.

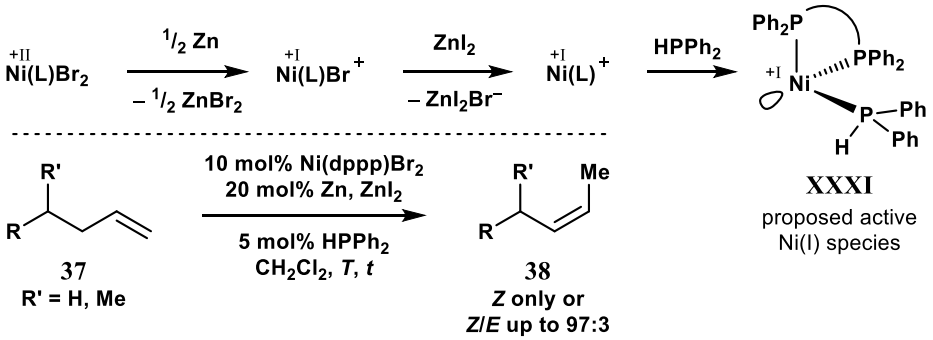
3. Results and Discussion

3.1 Nickel-Catalyzed *Z*-Selective Isomerization of Terminal Alkenes

The following chapters address the nickel-catalyzed *Z*-selective monoisomerization of terminal alkenes. The method was developed in the course of my Master thesis[102] together with Anastasia Schmidt. Mechanistic studies, revealing the stereochemical outcome of the reaction, as well as experiments concerning the elucidation of the active catalyst species will be discussed first. After that, the application of the isomerization reaction in natural product synthesis and multicomponent reactions will be presented.

3.1.1 Preliminar Studies

During my Master thesis,[102] the double bond isomerization with a catalytic system, consisting of the nickel precursor Ni(dppp)Br_2, Zn powder as reductant, the Lewis acid ZnI_2 and co-ligand diphenylphosphine ($HPPh_2$) was investigated and showed even better *Z*-selectivity than the similar reaction with the neighboring cobalt-based catalyst. Furthermore, the nickel catalyst featured an outstanding reactivity even at low temperatures as well as a high functional group tolerance.



Scheme 61: Formation of the proposed active Ni(I) species and *Z*-selective isomerization of terminal olefins.

The postulated paramagnetic reactive Ni(I) species **XXXI** (Scheme 61) is formed upon *in situ* reduction of the Ni(II) precursor with Zn and $HPPh_2$. The reduction process is apparently realized *via* electron transfer from Zn to the nickel center. During my Master thesis the substrate scope of the isomerization could already be explored. The reaction temperature and time had to be adjusted for each substrate to "find the right balance between reactivity and selectivity".[103] Further, the reaction needed to be stopped at the point where further conversion of the α-olefin lowered the amount of *Z*-isomer, because formation of the thermodynamically preferred *E*-isomer increased over time.[102] Figure 3 shows a selection of accessible *Z*-configured 2-alkenes.

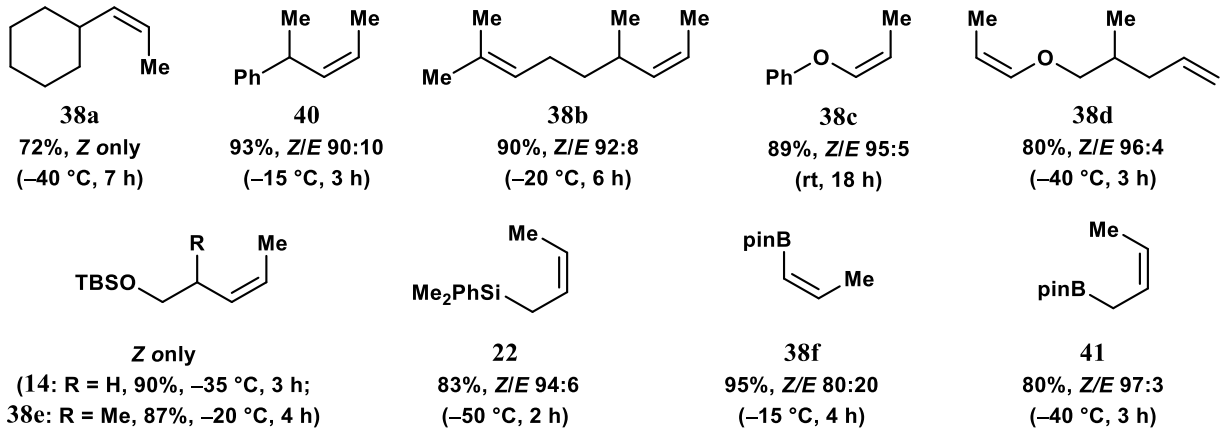
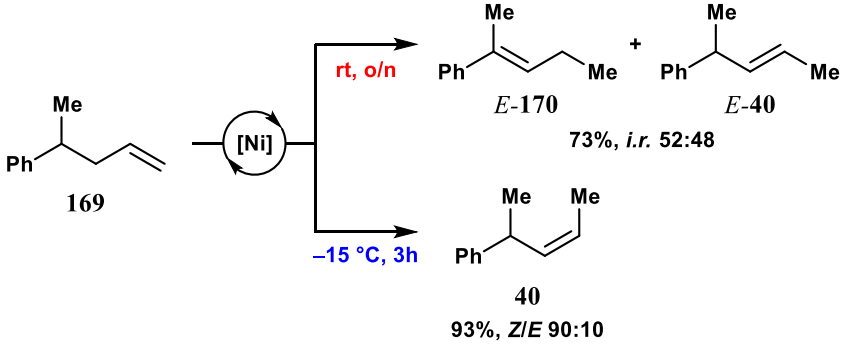


Figure 3: Substrate scope of the nickel-catalyzed monoisomerization of terminal olefins.

The main difference of the nickel catalyst compared with the cobalt catalyst is that chain walking can occur. When the nickel-catalyzed isomerization was performed at ambient temperature multiple double bond translocations took place at the expense of the reaction's selectivity. Thus, the thermodynamically equilibrated *E*-configured isomeric product mixture *E*-**170**/*E*-**40** was obtained (Scheme 62, top). By lowering the reaction temperature, the reactivity could be reduced in behalf of a good isomeric excess of the *Z*-configured 2-alkene **40** (Scheme 62, bottom).[102]



Scheme 62: Multiple 1,3-hydride shift (top) versus kinetic discrimination (bottom), (*i.r.* = isomeric ratio).

The transposition of the terminal double bond in **169** at ambient temperature is limited to two positions. Likewise, up to four isomers can be obtained. When 1-hexadecene was isomerized with the nickel catalyst at ambient temperature, a vast mixture of internal isomers could be detected *via* GC/MS analysis. Lowering the temperature to –40 °C, *Z*-configured 2-hexadecene could be obtained in a good *Z*/*E* ratio of 94:6 with 88% conversion, which again demonstrated the temperature-dependence of the nickel-catalyst's activity.[33,102] Instead, the cobalt catalyst isomerized the double bond over exactly one position, even at elevated temperatures. At a lower temperature (0 °C), the amount of *Z*-isomer increased, with very low conversion of the starting material, though.[33]

As described in chapter 1.2, chain walking occurs when a metal hydride species is present in the catalytic cycle of the reaction. An alkyl mechanism (Scheme 2) can therefore be expected for the nickel-based catalyst system with the hypothesis that the active catalyst species is a Ni(I) species formed by *in situ* reduction with Zn. Cyclic voltammetry (CV) and electron spin resonance (EPR) studies were performed. The postulated mechanistic suggestions were underlined by density functional theory (DFT) calculations.

3.1.2 Mechanistic Investigations

3.1.2.1 Cyclic Voltammetry

Cyclic voltammetry is of particular interest for the characterization of the active metal species in the double bond transposition. It is a reliable technique to acquire qualitative information about the transfer of electrons in organic molecules or transition metal complexes. The equipment required to perform CV consists of a conventional potentiostat connected to three electrodes (working, reference, and auxiliary electrode) immersed in a non-stirred solution. The potentiostat applies and maintains the potential between the working and reference electrode while at the same time measuring the current at the working electrode. Charge flows between the working electrode and the auxiliary electrode.[104] Triangular potential excitation signal sweeps the potential of an electrode between two values E_{min} and E_{max}. The scan rate ν is defined as potential change per time.[105]

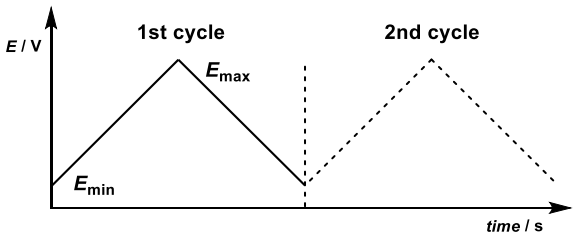


Figure 4: Triangular potential excitation for CV.

A current *I* flows through the electrode that either oxidizes or reduces the analyte. In our case, the catalyst M(dppp)Br_2 (with M = Co or Ni). The current density is plotted against the potential in the cyclic voltammogram and indicates the potential at which the redox process occurs.

Dichloromethane is the solvent of choice for the studies, since the target reaction, the isomerization, is also performed in this solvent. Dichloromethane is stable up to +3.0 V. As supporting electrolyte tetrabutylammonium tetrafluoroborate ($TBABF_4$) was chosen.

For all isomerization reactions, the catalyst is prepared according to a general procedure (GP), in the following known as GP 1: The catalyst precursor M(L)X_2 (with M = first row transition

metal, usually Co or Ni), Zn powder and ZnI_2 are dissolved in anhydrous dichloromethane. After 10 min, $HPPh_2$ is added as stock-solution and after additional 10 min the substrate is added at the desired temperature. In the first 10 min of stirring Hilt *et al*. propose the formation of a M(I)-species (with M = Co).[103] $HPPh_2$ acts as ligand and hydrogen donor to the substrate.[32] The preparation of the CV samples followed a similar procedure. Dr. Philipp Röse is thankfully acknowledged for his assistance.

When preparing the cobalt and nickel-based catalyst systems for CV measurement, the metal precursor M(dppp)Br_2 was suspended in a 0.1 M dichloromethane/$TBABF_4$ solution (2.5 mM with respect to metal precatalyst). In case of M = Co, the solution is always blue-green, in case of M = Ni it is red-brown. When Zn powder (2.0 eq with respect to metal precatalyst) was added, the mixture changed to darker green/brownish (Co) but remained unchanged for Ni. In both cases the addition of ZnI_2 (2.0 eq) had no more observable color change. The afore homogeneous solution showed schlieren when Zn and ZnI_2 were added. The most remarkable color change occured when $HPPh_2$ (0.5 eq in relation to the metal M) was added to the mixture. Either way, the color turned to dark red-brown as Figure 5 illustrates.

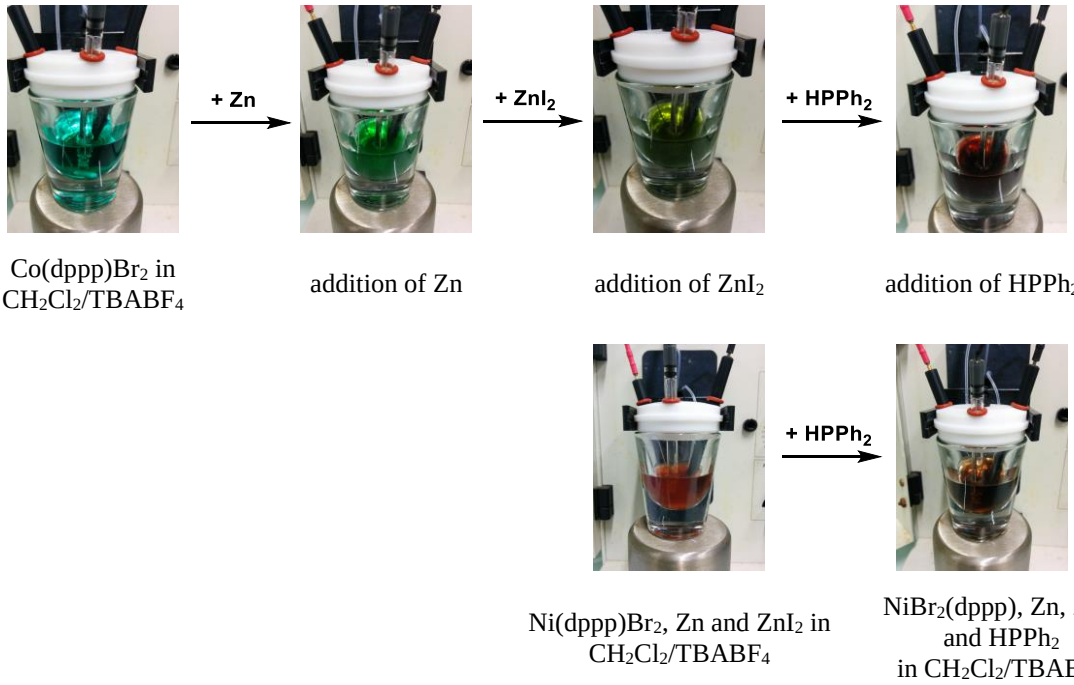


Figure 5: Pictures of the cobalt (top) and the nickel catalyst (bottom) solutions during CV measurements. CV was carried out on a BAS C3 Cell Strand and a BAS 100 series Electrochemical Analyzer using a platinum disk working electrode (2.0 mm diameter) and a platinum wire counter electrode (0.5 mm diameter) at ambient temperature in dichloromethane/$TBABF_4$ (0.1 M). Potentials were referred to a saturated Ag/AgCl reference electrode (3.0 M NaCl). Before each experiment the surface of the working electrode was polished followed by thorough rinsing with distilled water and the solution was purged with nitrogen.

Figure 6 shows the cyclic voltammograms for the reduction of the Co(II) precursor with zinc. The reduction potential of Co(II)/Co(I) is located at –0.74 V. The corresponding oxidation peak at 47 mV. When zinc is added to the solution, the reduction peak is diminished. This observation is in good accordance to the assumption that Co(II) is reduced to the Co(I) species by zinc. The reduction potential of Co(II)/Co(I) is a little shifted to –0.82 V compared to the voltammogram of pure Co(II) precursor, since zinc is also able to abstract a halide atom and can therefore slightly change the electronic properties of the precursor. When ZnI_2 and $HPPh_2$ are added, the characteristic peaks from Figure 6 (left side) vanish. Real reversible electron transfers could not be detected any longer. The small potentials of the dotted CV in Figure 6 (right side) could be an effect of traces of oxygen in the experimental setup, since a complete exclusion of air could not be guaranteed. Because of the moderate quality of the voltammograms, only a qualitative analysis is possible.

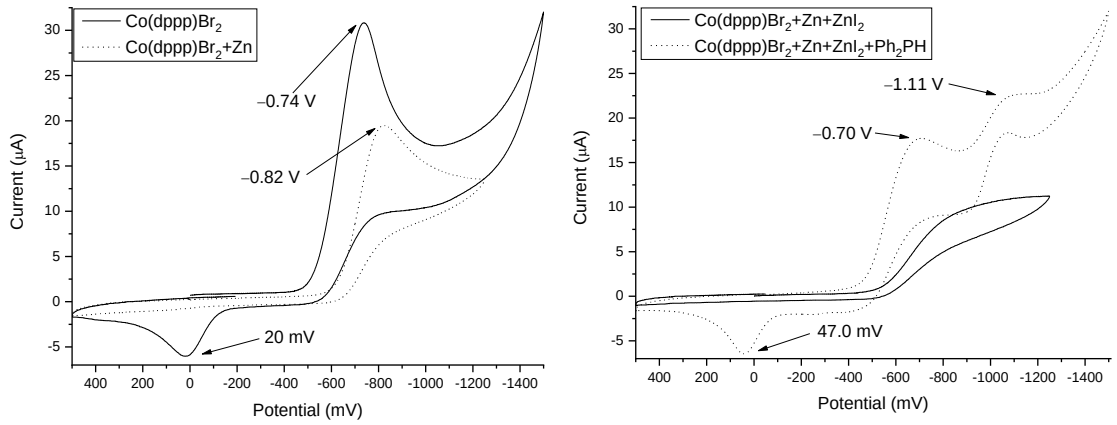


Figure 6: Cyclic voltammograms of $Co(dppp)Br_2$ (2.5 mM, 1.0 eq) in CH_2Cl_2/$TBABF_4$ (0.1 M) at ambient temperature using a platinum disc working electrode (0.5 mm diameter) with a scan rate of 100 mV/s. Potentials are referred to an Ag/AgCl reference electrode. (a) $Co(dppp)Br_2$; (b) in presence of Zn (2.0 eq); (c) in presence of Zn and ZnI_2 (2.0 eq each); (d) in presence of Zn, ZnI_2 (2.0 eq each) and $HPPh_2$ solution in CH_2Cl_2 (0.125 mM, 1.0 eq).

A major difference between the cobalt and nickel systems can be observed when comparing the cyclic voltammogram in Figure 6 with the one of the nickel precursor in Figure 7. The reduction peak of Ni(II)/Ni(I) at –0.61 V is not affected when Zn is added to the solution. With the addition of ZnI_2 the spectrum remains unchanged, too. Upon addition of $HPPh_2$, a reduction takes place, letting the reduction peak of Ni(II)/Ni(I) vanish to form the postulated active Ni(I) catalyst species. Again, a complete exclusion of air could not be guaranteed, what could explain the pseudo-reversible peaks of the dashed CV.

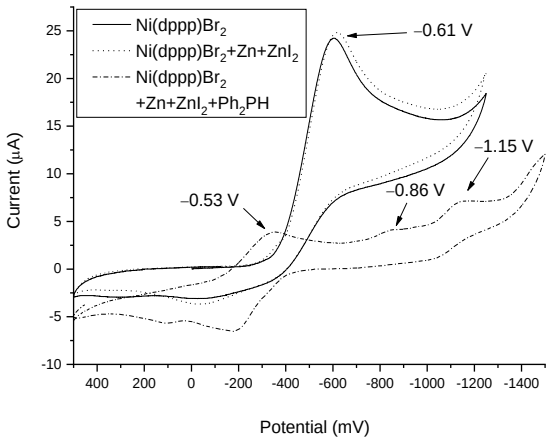


Figure 7: Cyclic voltammograms of Ni(dppp)Br_2 (2.5 mM, 1.0 eq) in CH_2Cl_2/Bu_4NBF_4 (0.1 M) at ambient temperature using a platinum disc working electrode (0.5 mm diameter) with a scan rate of 100 mV/s. Potentials are referred to an Ag/AgCl reference electrode. (a) Ni(dppp)Br_2; (b) in presence of Zn, ZnI_2 (4.0 eq); (c) a mixture of Ni(dppp)Br_2 (1.0 eq), Zn, ZnI_2 (4.0 eq) and $HPPh_2$ solution in CH_2Cl_2 (0.125 mM, 1.0 eq) were prepared in a separated heatgun dried Schlenk flask under argon atmosphere and diluted to the stated concentration followed by immediate measurement under nitrogen atmosphere.

As compared with literature data, the quasi-reversible wave reduction potential of Ni(II) to Ni(I) species is in the same range as the above measured values ($E_{1/2}$ = –0.84 V vs. Fc/Fc^+ for Ni(II)/Ni(I) in THF, respectively). Hillhouse *et al*. further describe the Ni(I)/Ni(0) transition to proceed with $E_{1/2}$ = 2.41 V.[106] The presence of a possible Ni(0) species can be excluded.

In summary, cyclic voltammograms of the Co(dppp)Br_2 complex changed significantly after addition of zinc powder and zinc iodide, indicating that the cobalt(II) precursor is easily reduced by zinc powder in the presence of a Lewis acid to the corresponding cobalt(I) complex. This change in oxidation state is visible by a distinct color change of the dichloromethane solution from green-blue to darker brownish-green. In contrast, the corresponding cyclic voltammograms of the nickel complex Ni(dppp)Br_2 exhibit no significant change after addition of Zn and ZnI_2.[103] However, after addition of $HPPh_2$ to this mixture, the reduction peak in the cyclic voltammograms vanishes, in combination with the observable characteristic color change from red to deep brown.

3.1.2.2 Electron Paramagnetic Resonance

From a mechanistic point of view, the reactive catalyst species is a nickel(I) complex with dppp and Ph_2PH in the ligand sphere. To confirm the CV experiments, further EPR spectra were measured under the supervision of Dr. Olaf Burghaus. As external standard for calibration DPPH (2,2-diphenyl-1-picrylhydrazyl) was utilized.

Frozen solutions of Ni(dppp)Br_2, Zn, ZnI_2 and $HPPh_2$ in dichloromethane were analyzed by EPR at either 130 K (nitrogen cooling) or 20 K (helium cooling). The left spectrum in Figure 8 shows the signal of a paramagnetic d^9-Ni(I) system for which a g-value of 2.181 could be calculated. The right spectrum has a rather broadened signal of the Ni(I) species.

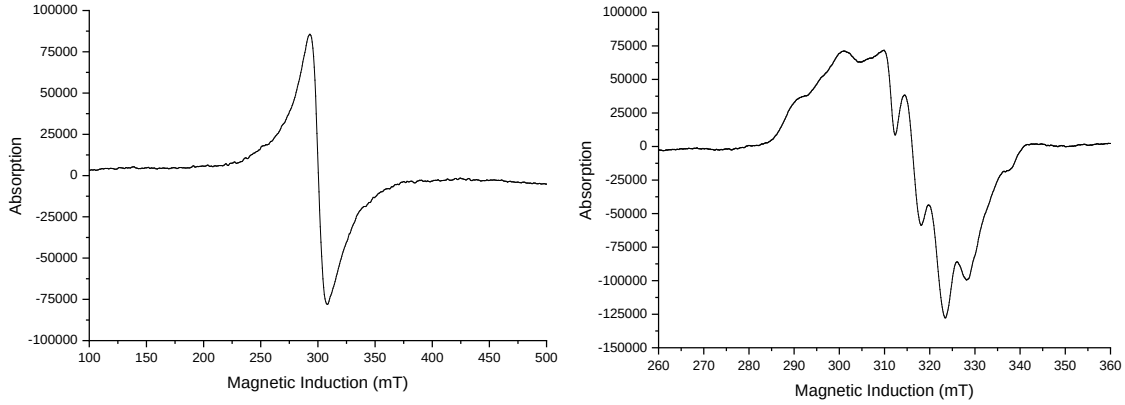
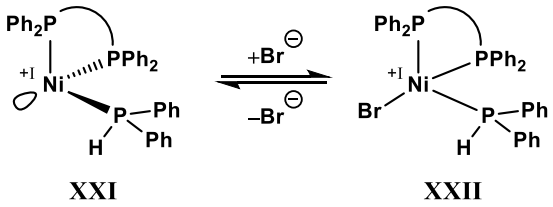


Figure 8: Left: X-band EPR spectrum (9.1581 GHz) of the active Ni^I-species Ni(dppp)Br($PHPh_2$), resp. Ni(dppp)$(PHPh_2)^+$ solution in CH_2Cl_2 (0.002 M) at 130 K (g = 2.1818). Right: X-band EPR spectrum (9.2469 GHz) of the active species in CH_2Cl_2 (0.01 M) at 20 K. For EPR measurement a mixture of Ni(dppp)Br_2 (1.0 eq), Zn, ZnI_2 (2.0 eq each) and $HPPh_2$ solution in CH_2Cl_2 (0.125 mM, 0.5 eq) were prepared in a separated heatgun dried Schlenk flask under argon atmosphere and diluted to the stated concentration followed by immediate measurement under argon atmosphere.

EPR measurements are inconclusive as an equilibrium between a square planar [Ni(I)(dppp)Br($PHPh_2$)] complex (**XXI**) or a cationic $[Ni(I)(dppp)(PHPh_2)]^+$ (**XXII**) species that could explain the hyperfine coupling pattern (Scheme 63).[103]



XXI **XXII**

Scheme 63: Postulated equilibrium between a square planar [Ni(I)Br(dppp)$(PHPh_2)$] complex or a cationic $[Ni(I)(dppp)(PHPh_2)]^+$ species.

A comparison with a simulated EPR spectrum (Figure 9) led to the conclusion that the presence of an additional bromide ligand is possible. It could be simulated with g tensor principal values of g_x = 2.2251, g_y =2.20706, and g_z = 2.00317.

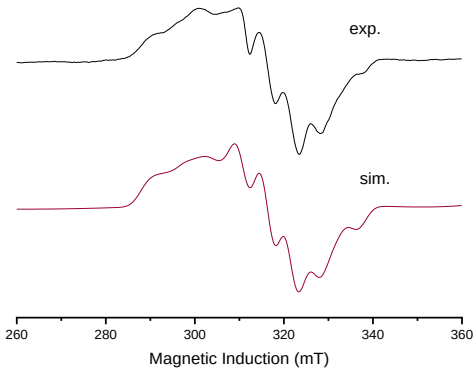


Figure 9: Top (black): X-band EPR spectrum (9.2469 GHz) of the active Ni(I)-species in CH_2Cl_2 (0.01 M) at 20 K. Bottom (red): Simulated EPR spectrum. Fits and simulations were carried out with the EPR data analysing program NSIMEPR using an orthorhombic spin Hamiltonian with hyperfine couplings calculated to second order. The fitting procedure is a simplex algorithm. Fits were started many times with different starting values and with different spin compositions. All parameters given here were allowed to relax free to the minimum. Best fit was obtained for three independent S = $^1/_2$ hyperfine couplings. The simulation was carried out by Dr. Olaf Burghaus.

The g values of d^9 transition metal ion centers are very sensitive to the coordination environment. The broadened line-widths could arise from the hyperfine couplings to the non-equivalent ^{31}P (I = $^1/_2$) nuclei (two for the dppp ligand and one for $PHPh_2$)[102] and to the ^{79}Br (I = $^3/_2$) nucleus.[107] This would mean either a four or a three-coordinate nickel atom is present. As can be compared to data for similar complexes in the literature.[108] Krossing *et al.* describe a four-coordinate d^9-$[Ni(dppp)_2Al(OR^F)_4]$ complex with similar three coordinate complexes.[109]

In conclusion, the postulated Ni(I) species could be identified *via* CV and EPR analysis which convinced us for determining a Ni(I) complex being the active catalyst species for the isomerization process.

3.1.2.3 Computational Investigations

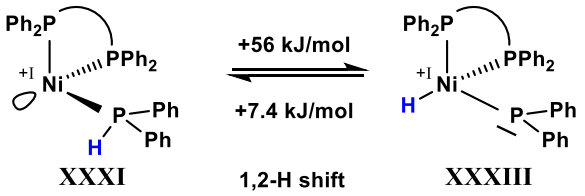
A computational study of the mechanism for the cobalt and nickel-catalyzed isomerization reactions was performed by Prof. Dr. Robert Berger and Evgeny I. Grigoryev in order to reveal the origin of the hydrogen and to determine the source of the *Z*-stereoselectivity. This chapter serves as an overview of the cooperation with the Berger group describing the general pathway of our postulated mechanism with potential differences to conventional alkyl and allyl mechanisms. More detailed computational data can be found in the corresponding literature.[110]

As EPR analysis revealed, the reaction is mediated by a square-planar [Ni(I)Br(dppp)($PHPh_2$)] complex or a cationic $[Ni(I)(dppp)(PHPh_2)]^+$ species. The reaction only proceeds in the presence of $HPPh_2$ in catalytic amounts as inherent part of the active catalyst species.

Alkyl Mechanism

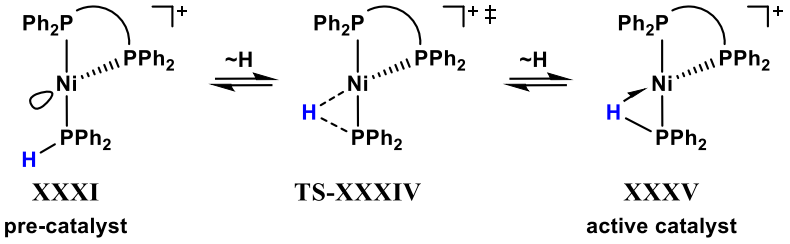
The isomerization reaction proceeds *via* a so-called alkyl mechanism for most terminal alkenes (for corresponding literature, see chapter 1.1.1). For the alkyl mechanism, usually a metal hydride species is necessary. As Hilt *et al.* described for the cobalt-catalyzed isomerization, they suggested the hydrogen being directly transferred from the $HPPh_2$ co-ligand to the substrate without an intermediary formed cobalt hydride species.[32,33] The same assumption was made for the nickel-based catalyst system.[102] The initial mechanistic proposal was investigated to reveal the role of $HPPh_2$, which is crucial for the reaction, because it acts as hydrogen source to initiate an isomerization *via* an alkyl pathway by transferring the hydrogen directly to the substrate.[32]

The catalytic cycle is initiated by a low barrier reversible 1,2-hydrogen shift. As can be seen in Scheme 3, the equilibrium is on the left side, since the activation barrier of 56 $^{kcal}/_{mol}$ for the 1,2-hydride shift is too high to actually form a real nickel hydride.[110]



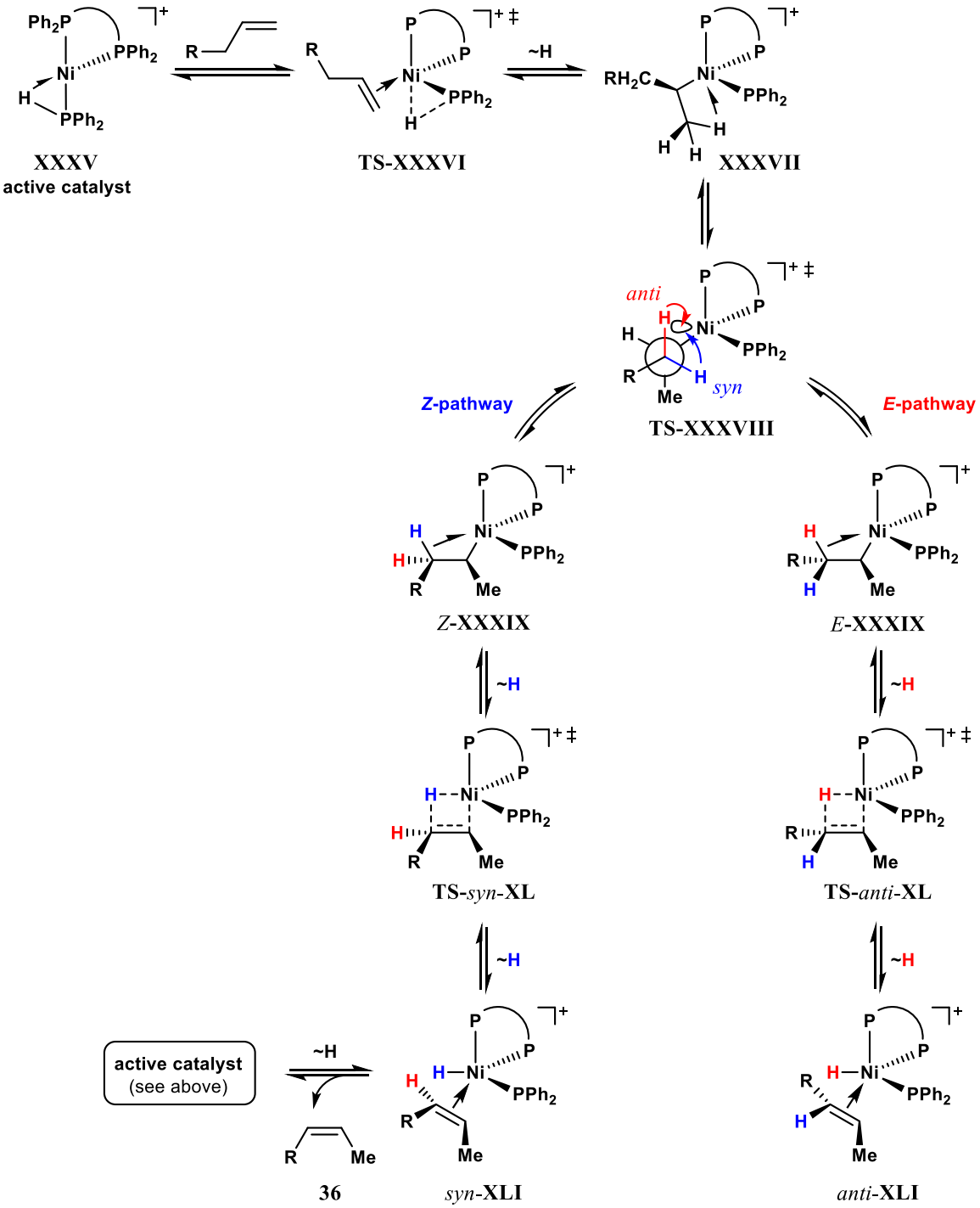
Scheme 64: 1,2-Hydride shift with calculated activation energies.

Depicted in Scheme 65, the α-agostically activated species **XXXV** acts as an active form of the catalyst. Complex **XXXI** is the pre-catalyst. Moreover, the active catalyst **XXXV** is not a true metal-hydrogen species, because it is stabilized by an α-agostic interaction with a bond order of 0.6 for P–H and 0.3 for H–Ni. The Ni–H–P arrangement is a three-center-two-electron bond.



Scheme 65: Formation of the active catalyst species **XXXV** (TS = transition state).

The catalytic isomerization of the terminal alkene is conducted by the $[(dppp)Ni\cdots H\cdots(PPh_2)]^+$ species **XXXV** which is activated for alkene insertion through an α-agostic interaction between the P–H bond of the $HPPh_2$ co-ligand and the nickel atom. The calculated mechanism is illustrated in Scheme 66.[110]



Scheme 66: Selected steps of the calculated alkyl mechanism for the *Z*-selective nickel-catalyzed isomerization. Selectivity arises on the stage of diastereomeric complex **XXXIX** (TS = transition state).

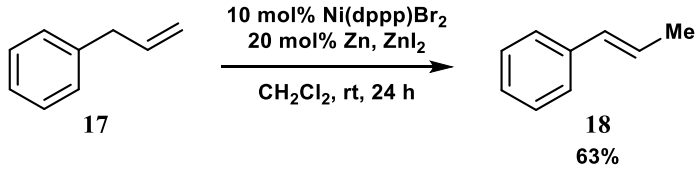
Upon coordination of the 1-alkene, in other words the formal 1,2-H-insertion into the α-agostically activated catalyst species **XXXVII**, the P–H bond breaks and a hydrogen transfer to the terminal olefinic CH_2-group leads to formation of a CH_3-group in **XXXIX** stabilized by β-agostic interaction. Then, a bifurcation of the reaction pathway takes place. The subsequent stereoselective β-H-elimination, running through the formal four-membered transition state TS-**XL**, provides the corresponding η^2- or π-complexes *E*-**XLI** and *Z*-**XLI**, respectively. **XLI** dissociates to release the *E*- and *Z*-configured 2-alkenes (shown for the *Z*-isomer **36** in Scheme 66) and can undergo another catalytic cycle after reversible 1,2-H-transfer back to the co-ligand.

Evgeny I. Grigoryev could show that the selectivity of the catalyst arises at the stage of the formation of the β-agostic complexes *E*-**XXXIX** and *Z*-**XXXIX**, which are diastereomeric to each other. Consequently, the *syn*/*anti*-notation can be used for the relative conformation of the substrate in the complex. The substrate has *anti*-conformation in *E*-**XXXIX** complex and *syn*-conformation in the *Z*-**XXXIX** conformer.

The *E*-configured 2-alkene **36** in free form is always thermodynamically more stable than the *Z*-configured counterpart. When they are bonded to the catalyst, though, the steric congestions around the nickel atom have to be considered. Because of the interaction between the substituent of the olefin and the bulky ligands, the β-hydride elimination becomes *Z*-selective.[110]

π-Allyl Mechanism for Allylbenzene

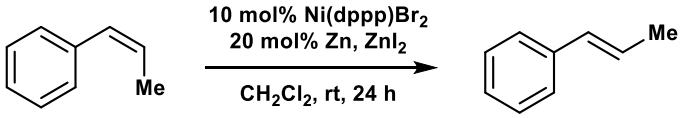
A major difference is given when allylbenzene (**17**) is isomerized. *E*-configured prop-1-en-1-ylbenzene (**18**) is always formed, not depending on the metal used. In case of M = Co this reaction only proceeds in the presence of $HPPh_2$. An interesting observation was made when isomerizing allylbenzene with the nickel catalyst without the use of $HPPh_2$.



Scheme 67: Nickel-catalyzed *E*-selective isomerization of allylbenzene without the use of $HPPh_2$.

As shown in Scheme 67, **17** was the only substrate which was isomerizable without $HPPh_2$. This observation led to the hypothesis that a different reaction pathway *via* π-allyl mechanism could be present when using the nickel-based pre-catalyst. To reveal this assumption,

Z-methylstyrene (*Z*-**18**) was isomerized to the corresponding *E*-isomer. Indeed, the reaction also succeeded without the use of the $HPPh_2$ co-ligand.

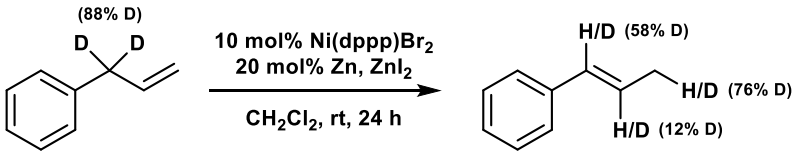


Z-**18** *E*-**18** 78%

Scheme 68: Nickel-catalyzed isomerization of *Z*-methylstyrene to *E*-methylstyrene without the use of $HPPh_2$.

The *Z*-configured 2-methylstyrene is presumably converted into the thermodynamically more stable *E*-isomer presumably *via* an allyl mechanism, which does not need any external hydrogen source. It requires one more vacant site on the nickel atom. This phenomenon was also described by Ong *et al*. for a tandem isomerization/C–H activation sequence.[111] Based on these results, Evgeny I. Grigoryev calculated activation barriers which fit to a formal 1,3-hydride shift running through η^3-nickel hydride intermediates *via* π-allyl mechanism (cf. Scheme 2 in chapter 1.1.1).

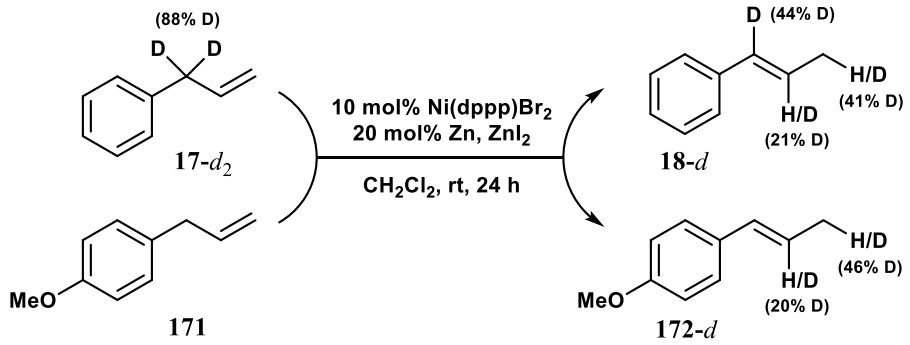
To confirm the proposed 1,3-hydride shift, deuterated allylbenzene (**17**-d_2) was isomerized (Scheme 69). As expected, the deuteride is incorporated to the terminal position of the substrate in 76%. 12% deuterium were further transferred to position 2.



17-d_2 **18**-*d* 68%

Scheme 69: Nickel-catalyzed *E*-selective isomerization of deuterated allylbenzene without the use of $HPPh_2$.

A crossover experiment using **17**-d_2 and non-deuterated 4-methoxyallylbenzene (**171**) revealed that a deuteride from the benzylic position is also incorporated in the second substrate after isomerization (Scheme 70).



Scheme 70: Crossover experiment with deuterated allylbenzene and 4-methoxyallylbenzene.

46% deuterium were incorporated to the methyl group of **172**, whereas 44% remained at the benzylic position of **18**-*d*. Additionally, around 20% deuterium were transferred to position 2 of each product.

The nickel catalyst is able to abstract a deuteride to transfer it to the second starting material during the isomerization process. This observation led to the idea of an alkyl mechanism with allylic activation. The isomerization of allylbenzene derivatives could therefore proceed *via* both mechanisms. Further mechanistical calculations concerning the isomerization of allylbenzene are currently underway.

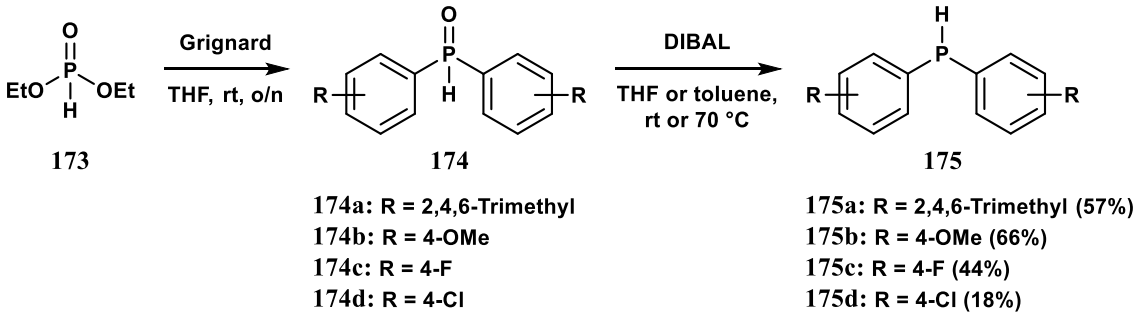
In summary, the β-hydride elimination determines the high *Z*-selectivity. For most terminal alkenes (except for allylbenzene) the reaction follows the pathway of a conventional alkyl mechanism. The co-ligand $HPPh_2$ is required for the initial transfer of the hydrogen atom to the substrate without the formation of a real nickel hydride species. The steric congestion around the nickel atom stabilizes the substrate in a *syn*-conformation that provides a high *Z*-stereoselectivity. The nickel-catalyzed isomerization of allylbenzene proceeded *E*-selectively in the absence of $HPPh_2$ and could follow an alkyl mechanism with allylic activation. The cobalt-catalyzed isomerization does not give any conversion in the absence of $HPPh_2$.

The cooperation with the Berger group underlined the "substrate-dependent mechanistic diversity" of the nickel-catalyzed isomerization.[110]

3.1.3 Isomerization with Diphenylphosphine Derivatives

Diphenylphosphine acts as the crucial additive concerning reactivity and selectivity of the cobalt and nickel-based catalyst system providing the necessary hydrogen atom for the above verified alkyl mechanism. Corinna Kohlmeyer already addressed different hydrogen sources for the formation of the active nickel catalyst species, such as water, acids, silanes and amines

in her Master thesis.[112] Therefore, these additives will not be features in this chapter. At this point, one last issue shall be clarified, whether the electronic and steric configuration of the phosphine additive have a measurable impact on the catalyst's reactivity and the *Z*-selectivity of the isomerization. For this purpose, differently substituted $HPPh_2$-derivatives were synthesized according to a procedure of Busacca together with Lukas Alig (Scheme 71).[113]

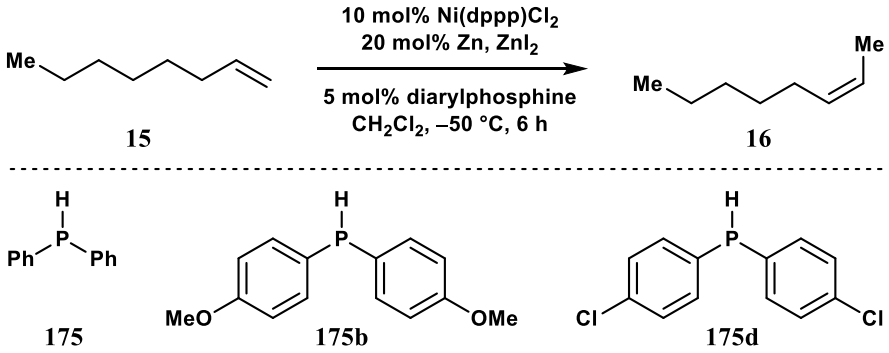


Scheme 71: Synthesis of substituted $HPPh_2$-derivatives with overall yield.

The target molecules are addressable *via* Grignard reaction of diethyl phosphite (**173**) and the corresponding aryl bromide. The second step comprises the reduction of the aryl phosphite **174** with di*iso*butyl aluminum hydride (DIBAL). The secondary phosphines of type **175** are very air-sensitive. During the preparation and storage, it has to be made sure, that the product is not exposed to air. All compounds could be synthesized in acceptable overall yields of up to 66% in two steps.

The application of the secondary phosphines in the *Z*-selective isomerization reaction should reveal, if the reactivity and especially the *Z*-selectivity of the established nickel-based catalyst system can be correlated to the electronic nature of the phosphines. Hopefully, an even better selectivity can be reached by varying the substituent on the phenyl moiety. The preparation of the catalyst was carried out according to GP 1 described in chapter 1.2.1. All reactions were compared to those performed with commercially available $HPPh_2$.

1-Octene (**15**) was used as first test substrate for the *Z*-selective isomerization at –50 °C with either $HPPh_2$, the electron-rich bis(4-methoxyphenyl)phosphine **175b**, or the rather electron-deficient bis(4-chlorophenyl)phosphine **175d**. The reaction is shown in Scheme 72.



Scheme 72: Isomerization of 1-octene with three different phosphines.

The phosphine was added as stock solution (0.125 mM in dichloromethane) at ambient temperature and the mixture was stirred for another 10 min, until being cooled to –50 °C. 1-Octene was then added and reaction samples were taken after defined times. GC analysis was performed for a determination of the conversion of the starting material, the *Z*/*E*-ratio of 2-octene as well as the amount of other internal isomers formed at this temperature. The use of an internal standard was not necessary, since only the conversion of the starting material should be determined. The time course of the reaction obtained with the three phosphines are plotted in Figure 10.

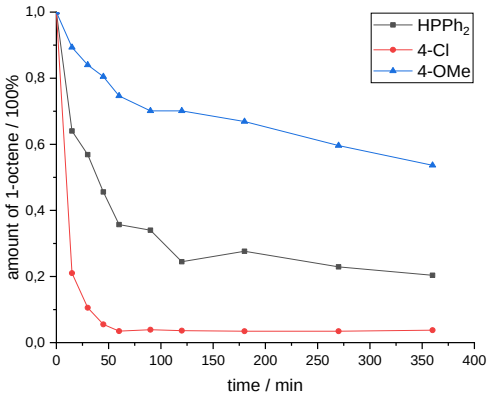


Figure 10: Normalized conversion of 1-octene in dependence of time for different phosphines.

When $HPPh_2$ was used as co-ligand, the conversion of 1-octene was not complete. It reached the plateau of around 80% conversion after 6 h reaction time (black line in Figure 10). An outlier was measured at t = 180 min. The reaction with 4-chlorophosphine **175d** was already completed within an hour with a maximum conversion of 96% (red line). As can be seen above, 4-methoxy-substituted phosphine **175b** reacts very poorly with the substrate. Even after 6 h reaction time, the conversion of 1-octene has not even reached 50%. The experiment is an average of two runs. Compared to the other phosphines, 4-chlorophosphine **175d** works best in terms of reactivity. Figure 7 illustrates the *Z*/*E*-ratio of 2-octene (**16**) and the number of other

isomers formed in the process. Because of its low reactivity, the 4-methoxy-substituted phosphine **175b** was no more considered for this examination.

As can be seen in Figure 11, in terms of *Z*-selectivity $HPPh_2$ (left diagram) is superior to its 4-chloro-substituted counterpart (right diagram). A *Z*/*E* ratio of around 3:1 could be obtained with $HPPh_2$ as co-ligand at a reaction temperature of –50 °C after 6 h reaction time. The 4-chlorophosphine **175d** provided a *Z*/*E* ratio of 2.5:1 with a significant higher amount of other internal isomers (right side, blue curve). The high reactivity of phosphine **175d** provides a lack in selectivity, though.

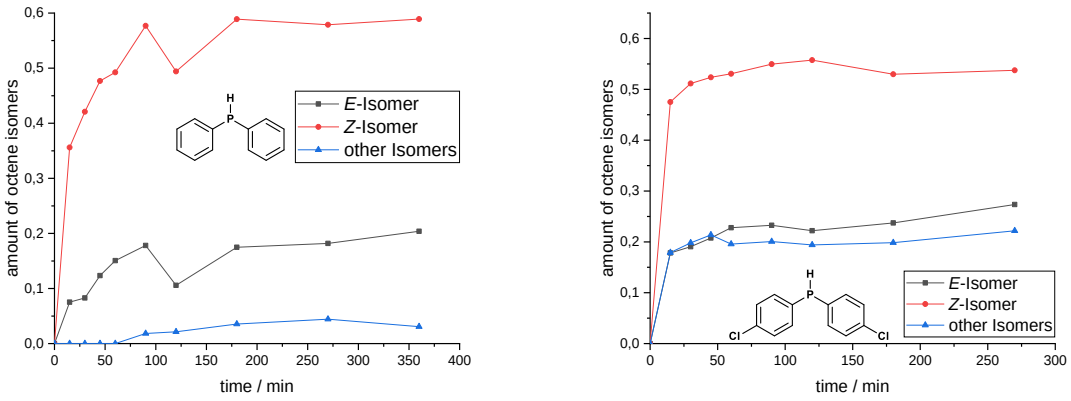
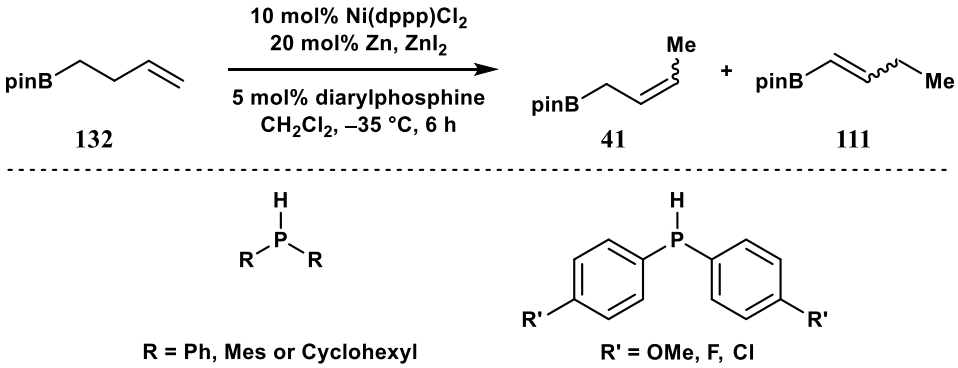


Figure 11: Amount of internal octene isomers for the isomerization with $HPPh_2$ (left) and bis(4-chlorophenyl)-phosphine (right).

Since 1-octene gave too many internal isomers at –50 °C, the reaction was difficult to be plotted accurately. The target substrate was therefore changed to boronic ester **132**, which is easier to handle in the isomerization reaction and the amount of other internal isomer is limited to one, the vinyl boronic ester **111** (cf. Scheme 73).



Scheme 73: Isomerization of homoallyl boronic acid pinacol ester **132** with different phosphine additives.

Furthermore, the peaks in the gas chromatogram of the possible isomers are better baseline separated compared to those of the octene isomers, so a better integration is provided and monitoring of the reaction *via* GC analysis was way easier.

The reaction shown in Scheme 73 was performed under the established conditions utilizing 5 mol% phosphine. The appropriate plot is shown in Figure 12.

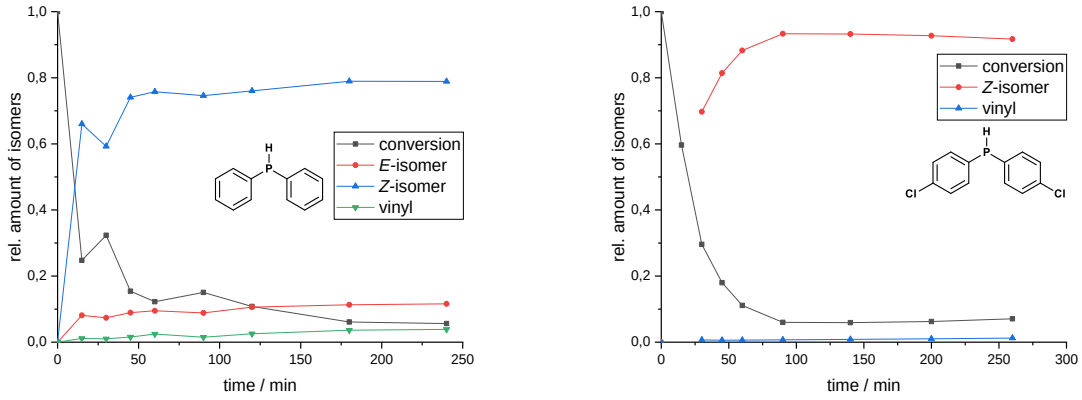


Figure 12: Comparison of the isomerization with $HPPh_2$ (left) and bis(4-chlorophenyl)phosphine (right).

Interestingly, the isomerization with 4-chloro phosphine **175d** in Figure 8 (right diagram) shows an excellent reactivity and *Z*-selectivity at –35 °C reaction temperature. Nearly no *E*-isomer can be detected *via* GC analysis, albeit the amount of vinyl boronic ester **111** increases slightly in the course of time. The isomerization of the *Z*-configured crotyl boronic ester **41** to the vinylic species **111** proceeds faster than the competing *Z* to *E* isomerization of the double bond located in the allylic position. The isomerization of **132** with other phosphines is depicted in Figure 13. Only low and therefore not satisfying conversion of the starting material is observed, which is also already illustrated above when 1-octene was used as terminal alkene. Electron-rich phosphines, such as the mesityl- (**175a**), the 4-methoxy- (**175b**), or the cyclohexyl-substituted one are not suited to catalyze the isomerization reaction effectively. Also, bis(4-fluorophenyl) phosphine **175c** was completely unreactive. These phosphines do not seem to be the ones of choice for the isomerization process.

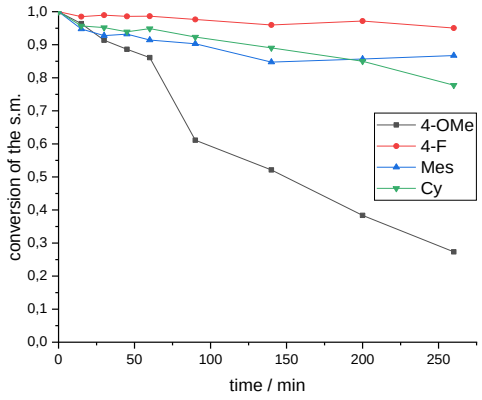


Figure 13: Isomerization of homoallyl boronic ester **132** with bis(cyclohexyl)phosphine (green line), bis(4-fluorophenyl)phosphine (red line), bis(4-methoxyphenyl)phosphine (black line) and bis(mesityl)phosphine (blue line) with no satisfying conversion of the starting material (s.m.).

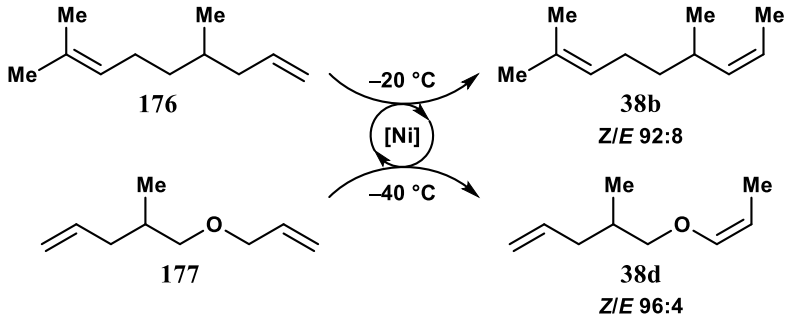
In summary, a screening of different secondary phosphines came to the result that outstanding reactivity could only be accomplished with simple $HPPh_2$ and bis(4-chlorophenyl) phosphine. The phosphine screening was performed for two substrates: 1-octene (**15**) and homoallyl boronic ester **132**. A correlation between electronic structure or steric factors and the reactivity and *Z*-selectivity of the phosphines applied could not be detected. Electron-rich phosphine do not show any reactivity. Alone, bis(4-chlorophenyl) phosphine shows a higher reactivity and in case of boronic ester **132** a better *Z*-selectivity than commercially available $HPPh_2$. In case of 1-octene $HPPh_2$ was still the additive of choice, because of its outstanding selectivity. Bis(4-chlorophenyl) phosphine could act as possible surrogate for future transformations with selected substrates. Since simple $HPPh_2$ is commercially available and easier to handle and store, it will still be the phosphine of choice for all the future transformations *via* nickel-catalyzed isomerization. The chloro-substituted phosphine **175d** can be kept in mind for special substrates whose reactivity and *Z*-selectivity is not satisfying enough when $HPPh_2$ is applied.

3.1.4 Application of the Z-Selective Isomerization in Natural Product Syntheses

3.1.4.1 Isomerization of α,ω-Dienes

Simple aliphatic, branched, and functionalized α-olefins could already be addressed *via* nickel-catalyzed diphenylphosphine-assisted *Z*-selective isomerization. Through targeted adjustment of the reaction temperature, a regioselective isomerization of substrates with a second internal or terminal double bond present in the molecule, was achieved. An additional trisubstituted internal double bond remained untouched by the catalyst (Scheme 74, top), even at ambient

temperature. When a second terminal double bond was present in the starting material, a kinetic discrimination of the sterically more shielded double bond was only achieved at a temperature low enough for the monoisomerization of the better accessible one (–40 °C, Scheme 74, bottom). At higher temperatures the competing double bond of **177** was also isomerized, which leads to a dramatic loss in regioselectivity.[102]



Scheme 74: Kinetic discrimination of terminal and internal double bonds at low temperatures.

Diene subunits are a common structure motif in several natural products and pharmaceutically active compounds, especially in insect attractants and pheromones.[114,115] Figure 14 illustrates a selection of natural compounds with a conjugated or skipped diene structure motif, which are sexual hormons of the beet armyworm *spodoptera exigua* (9*Z*,12*Z*-**165**), and Indianmeal moth *plodia interpunctella* (9*E*,12*Z*-**165**). Furthermore, the natural product aucanthen (**180**) is an odorous substance of the marine brown alga *cutleria multifida*.[116] The molecule contains two double bonds in close proximity to each other. The molecules, shown in Figure 14, are natural products potentially addressable by the nickel-catalyzed monoisomerization. All substances contain a double bond next to a methyl group. By targeted temperature adjustment, either an *E*- or a *Z*-configured double bond can be formed according to which stereoisomer of the pheromone is desired.

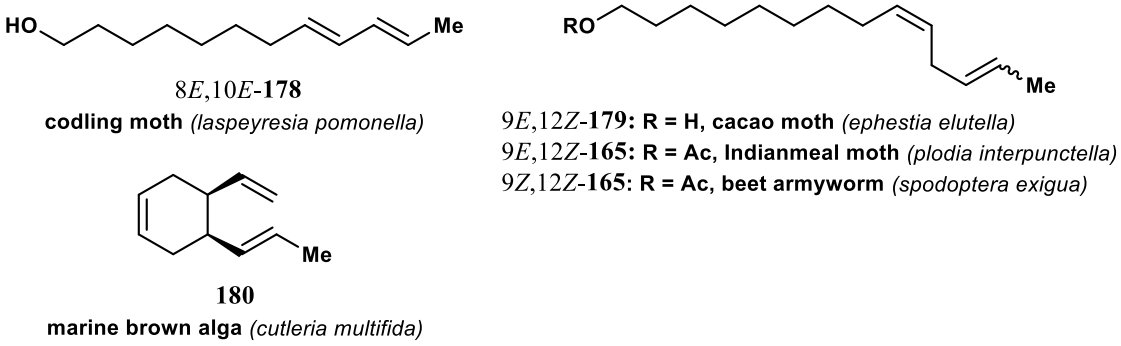


Figure 14: Aucanthen (**180**) and selection of insect pheromones with 8,10- and 9,12-diene substructure.

3.1.4.2 Pheromone Syntheses

For the synthesis of the desired diene structures, our synthetic approach contained a threefold challenge in the final isomerization step. The catalyst should generate the double bond in position 2 (highlighted in green in Figure 15) with high *Z*-selectivity without converting the skipped diene subunit into a conjugated system and the configuration of the internal double bond should not be altered by the catalyst.[103] Figure 15 illustrates the challenges for a selective double bond migration using the example of the pheromone (9*Z*,12*Z*)-tetradeca-9,12-dien-1-yl acetate (**165**), one of the sexual hormone ingredients of the beet armyworm *spodoptera exigua*.

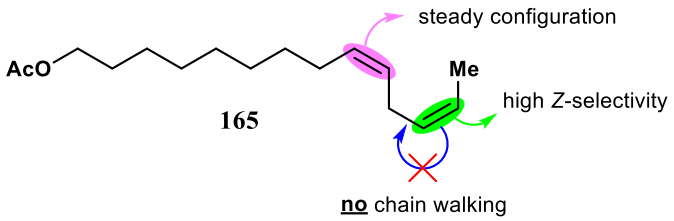
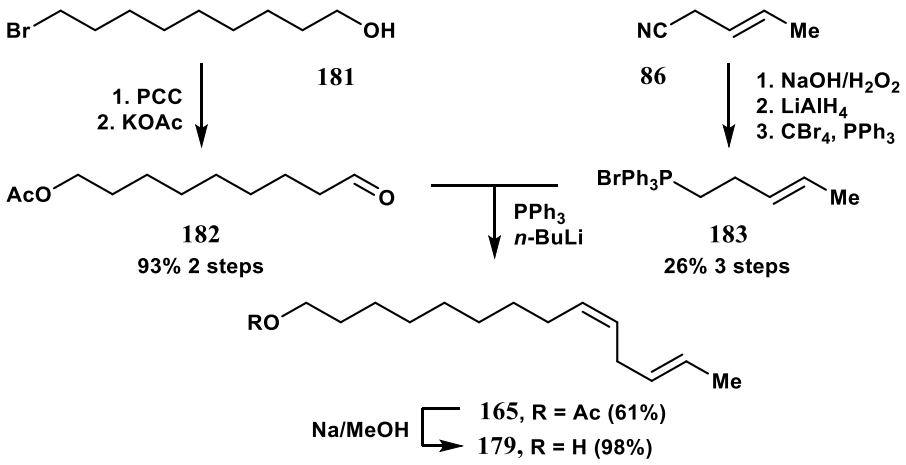


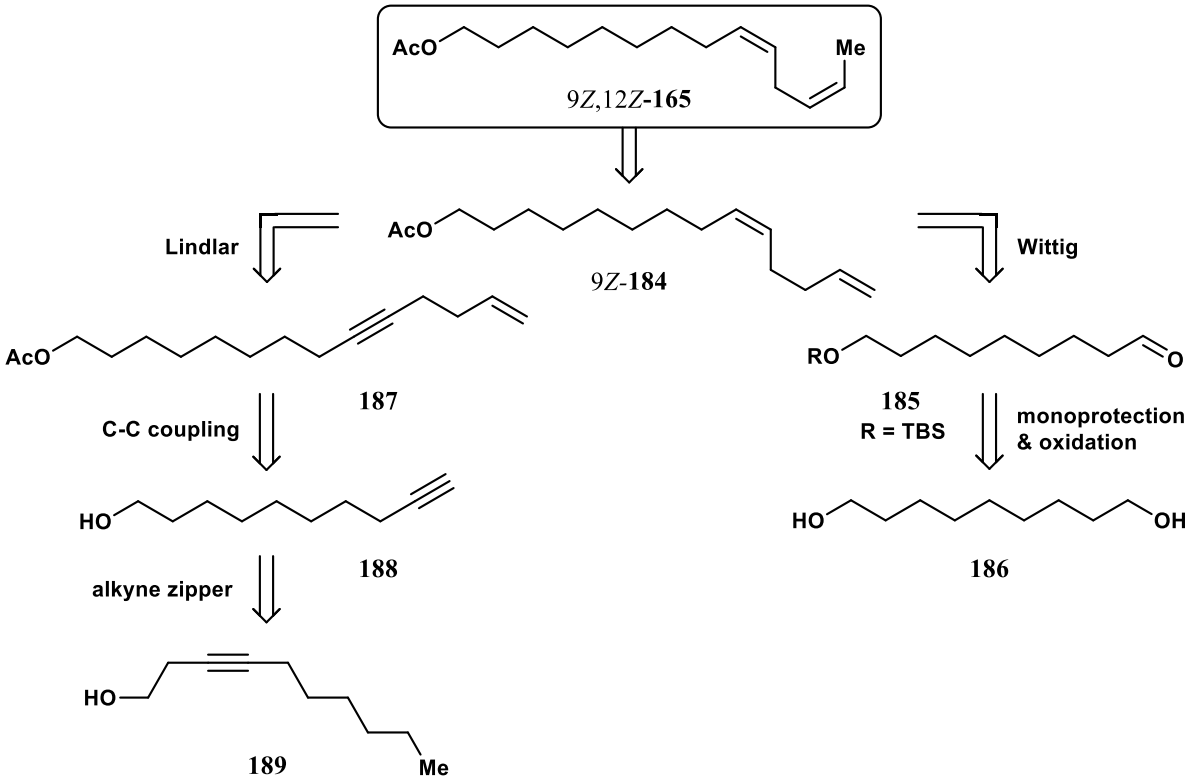
Figure 15: Challenges for a selective double bond isomerization.

In a 2013 report, Grubbs highlighted the cross-metathesis reaction as an alternative convenient method for the preparation of *Z*-configured internal double bonds applicable in pheromone syntheses.[114] Ortiz and co-workers could get access to (9*Z*,12*E*)-tetradeca-9,12-dien-1-yl acetate, the sex pheromone of the olive pyralid moth *euzophera pinguis* and the corresponding *E*-isomer of target molecule **165**. They formed the internal *Z*-configured double bond *via* Wittig olefination of linear aldehyde **182** and pent-3-enyltriphenylphosphonium bromide (**183**) starting from commercially available nitrile **86** (cf. DuPont Adiponitrile Process in Scheme 32) and bromide **181** as Scheme 75 reveals.[117]



Scheme 75: Pheromone synthesis by Ortiz and co-workers.

The own synthetic approaches towards the total synthesis of the C14-pheromone (9*Z*,12*Z*)-tetradeca-9,12-dien-1-yl acetate (**165**) shall start from commercially available starting materials **186** or **189** (Scheme 76) with either a subsequent Wittig olefination or Lindlar hydrogenation for the stereoselective formation of the *Z*-configured internal double bond. The syntheses shall be completed with a final *Z*-selective isomerization of alkene **184** as key step.



Scheme 76: Planned approaches towards the starting material for the pheromone synthesis through a final *Z*-selective isomerization step.

The second target structure, the C12-pheromone pheromone (8*Z*,10*Z*)-dodeca-8,10-dien-1-yl acetate (**164** in Figure 16) should be addressable according to the same pathway.

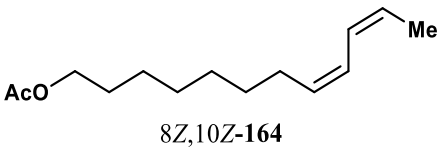
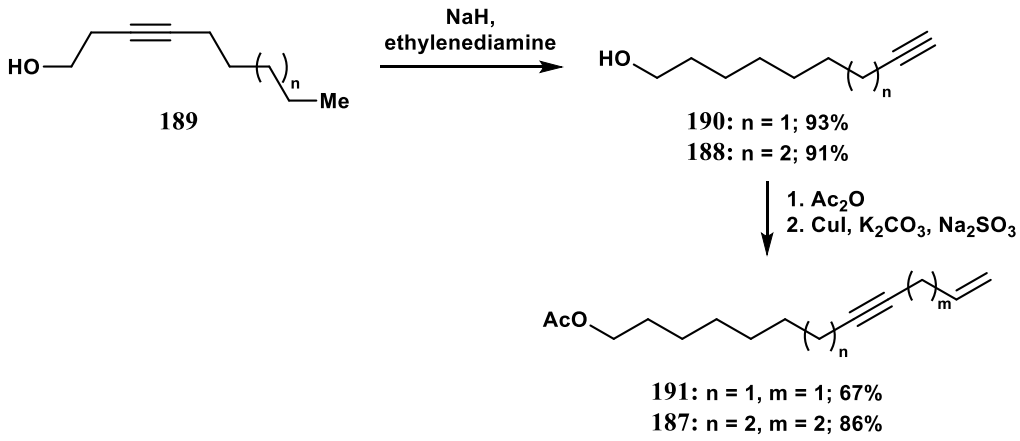


Figure 16: Target structure of the pheromone (8*Z*,10*Z*)-dodeca-8,10-dien-1-yl acetate (**164**).

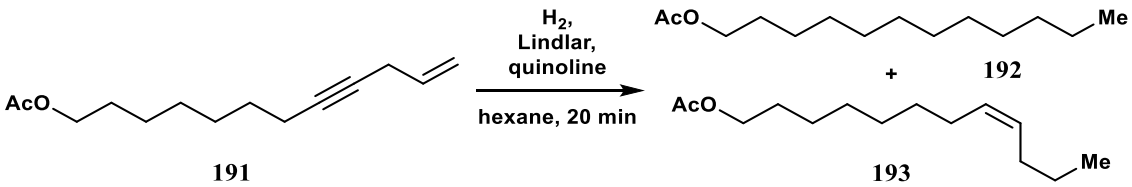
The initial synthetic approaches towards all-*Z*-configured pheromones **164** and **165** started with an alkyne zipper reaction of internal alkyne **189**, which Anastasia Schmidt also applied in her total synthesis of *O*-protected urushiol.[92] The literature-known[118] formation of terminal alkynes **188** and **190** proceeded easily in good yield (93% in case of the C-9 alcohol and 91% in case of the C10-alcohol). Subsequent acetyl protection and copper-catalyzed C-C-bond coupling of

the terminal alkynes with the corresponding (homo)allylbromide could be realized according to a procedure of da Silva in good yields (Scheme 77).[119]



Scheme 77: Zipper reaction and C-C-coupling for enyne synthesis.

With the acetyl-protected enynes **187** and **191** in hand, the triple bond reduction in *Z*-selective fashion should be accomplishable through Lindlar hydrogenation according to a procedure of Ghasemi.[118] Unfortunately, the hydrogenation with a Pd/C-catalyst presumably formed the completely hydrogenated product **192** or the catalyst hydrogenated both, the alkyne moiety to the alkene as well as the terminal double bond to saturation. The undesired products could be verified by GC/MS analysis and NMR spectroscopy. A higher loading of the catalyst poisons $Pb(OAc)_2$ and quinoline or a shorter reaction time resulted in no conversion at all.

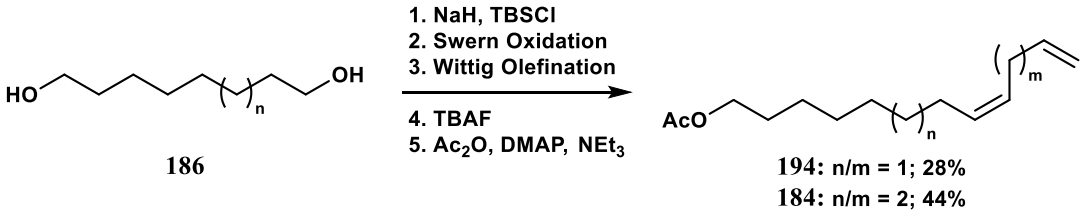


Scheme 78: Unselective Lindlar hydrogenation of enyne **191**.

The Lindlar hydrogenation was also unsuccessful for the free alcohol of **191** and the TBS-protected alcohols. No regiodifferenciation between a terminal double bond and the internal, more reactive internal triple bond occurred.

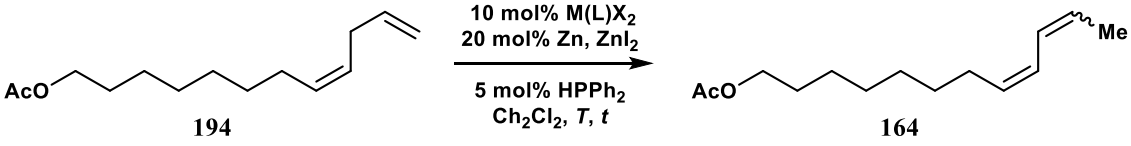
The second approach (Scheme 76, right side) included the formation of the *Z*-configured internal double bond *via* Wittig olefination. The synthesis started with a TBS-protection and oxidation of commercially available diols **186** (n = 1 or 2, Scheme 79). The resulting aldehydes were olefinated by a Wittig reaction with homoallyl or and 1-pentenyl-triphenylphosphonium bromide, respectively. The acetal group had to be introduced after the Wittig reaction, since the ester moiety inhibited the desired carbonyl olefination. Subsequent desilylation with

tetrabutylammonium fluoride (TBAF) and ester formation yielded the desired 1,4-diene **194** and 1,5-diene **184** in acceptable yields over five linear steps, which could then be introduced for the final regioselective isomerization key step. The precursor synthesis is summarized in Scheme 79.



Scheme 79: Synthesis of the pheromone precursors *via* alcohol oxidation/Wittig olefination sequence.

The final isomerization step was achieved by initial reaction condition screening, such as metal (Co or Ni), phosphine ligand, and temperature for both target molecules, C12-pheromone **164** and C14-pheromone **165**.



Scheme 80: Desired *Z*-selective isomerization of the pheromone precursor **194**.

The modifications for the C12-pheromone with 2,4-diene substructure **164** will be presented first. Table 1 summarizes the optimization of the reaction conditions.

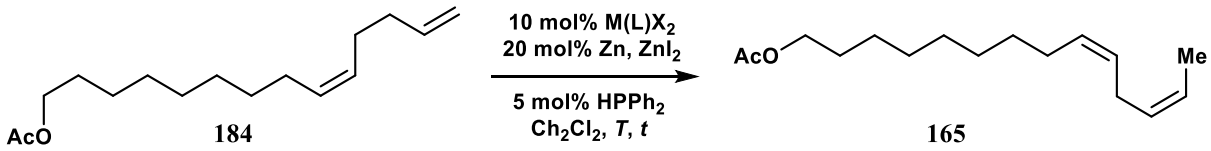
Table 1: Screening for conditions for the isomerization of the 1,4-diene subunit of **194**.

entry	M(L)X2	*T*, *t*	reaction progress[a]
1	Ni(dppp)Br2	rt, 18 h	*E*/*Z* 73:27 incomplete conversion
2	Ni(dpppBuEt)Br2	rt, 18 h	low conversion
3	Ni(dppe)Cl2	rt, 18 h	*E*/*Z* 70:30 incomplete conversion
4	Ni(dppe)Cl2	rt, 4 d	77% yield, *E*/*Z* 50:50
5	Ni(bdpp)Br2	rt, 2 d	*E*/*Z* 37:63 incomplete conversion
6	**Co(dppp)Br2**	**rt, 18 h**	**90% yield, *E*/*Z* 87:13**
7	Co(dppp)Br2	0 °C, 18 h	no conversion

a: General reaction conditions: M(L)X2 (10 mol%), Zn, ZnI2 (20 mol% each), HPPh2 (5 mol%) in CH2Cl2 (0.1 M), 10 min stirring at rt, then addition of the 1,4-diene **194** (1.0 M) and stirring at rt for the desired time.

Most of the time, the isomerization with a nickel-based catalyst provided incomplete conversion and a *Z*/*E* mixture of the resulting 1,3-diene. Especially at lower temperatures (< 0 °C, or < rt) the reaction did not proceed. After increasing the temperature to ambient temperature and adding another portion of catalyst, the conversion could be completed, but the *Z*/*E* ratio was not further improved (entries 4+5). The isomerization with the cobalt-based catalyst Co(dppp)Br_2 gave full conversion with mainly *E*-selectivity (entry 6). Lowering the temperature resulted, again, in no conversion of the starting material **194** (entry 7). For the 1,3-diene structure, the *E*-isomer was the thermodynamically favored product. Either way (use of Ni, and Co-catalyst), the configuration of the internal double bond was not altered. The synthesis of the *Z*,*Z*-configured product **164** did not succeed, but the corresponding *Z*,*E*-configured isomer could be obtained in a good isomeric excess (*ie*) of 74% and an excellent yield of 90%.

In case of the 1,5-diene precursor **184**, the nickel-catalyzed isomerization was easier to handle, since it proceeded smoothly at lower temperatures. The conversion could be controlled by targeted adjustment of the reaction temperature. The reaction proceeded slower and was better monitorable.



scheme 81: Final isomerization step in the total synthesis of C14-pheromone **165**.

Table 2 summarizes the optimization of the reaction conditions.

Table 2: Reaction condition screening for the isomerization of the 1,5-diene subunit of **184**.

entry	M(L)X_2	*T* / *t*	reaction progress[a]
1	Ni(dppp)Br_2	rt, 1 h	unselective reaction
2	Ni(dppp)Br_2	–30 °C, 4 h, → rt, o/n	*Z*/*E* 83:17
3	Ni(dppp)Br_2	–50 °C, 18 h	low conversion
4	Ni(dppp)Br_2	–15 °C, 8 h	92% yield *Z*/*E* 83:17
5	**Ni(dppe)Cl_2**	**–15 °C, 8 h**	**92% yield *Z*/*E* 88:12**

a: General reaction conditions: Ni(L)X_2 (10 mol%), Zn, ZnI_2 (20 mol% each), $HPPh_2$ (5 mol%) in dichloromethane (0.1 M), 10 min stirring at rt, then addition of the 1,5-diene **184** (1.0 M) and stirring at rt for the desired time.

The isomerization with the usual nickel-catalyst Ni(dppp)Br_2 at ambient temperature resulted in the formation of an undefined mixture of internal diene isomers, which could be detected *via* GC/MS analysis and were not further characterized (Table 2, entry 1). The isomerization gave

full conversion, though. The temperature was decreased to −30 °C to slow down the reaction and decrease the number of isomers to the desired 2,5-diene substructure (entry 2). Warming up the reaction overnight to ambient temperature resulted in a *Z*/*E* mixture of 83:17 with nearly quantitative consumption of the starting material **184**. A further decrease in temperature (−50 °C, entry 3) resulted in incomplete conversion of the starting material. Best results were obtained at −15 °C and 8 h reaction time to prevent the 2-*Z*-double bond from further chain walking or isomerizing to the *E*-isomer. Switching the ligand from dppp to dppe gave an increase in selectivity to the best achievable *Z*/*E*-ratio of 88:12. Pure (9*Z*,12*Z*)-tetradeca-9,12-dien-1-yl acetate (**165**) could be isolated *via* $AgNO_3$-impregnated silica flash column with a stepwise solvent gradient. Further information can be found in the experimental section.

In summary, the C12-pheromone with the conjugate diene structure motif (**164**) could be obtained in 90% yield and 74% isomeric excess of the *E*-configured double bond in position 2. An isomerization to the initially desired *Z*,*Z*-configured isomer was not possible, whereas the C14-pheromone from *spodoptera exigua* **165** could be easily obtained by nickel-catalyzed isomerization of the corresponding 1,5-diene **184** at −15 °C in excellent yield (92%) and high isomeric excess (76%) of the desired *Z*,*Z*-configuration.

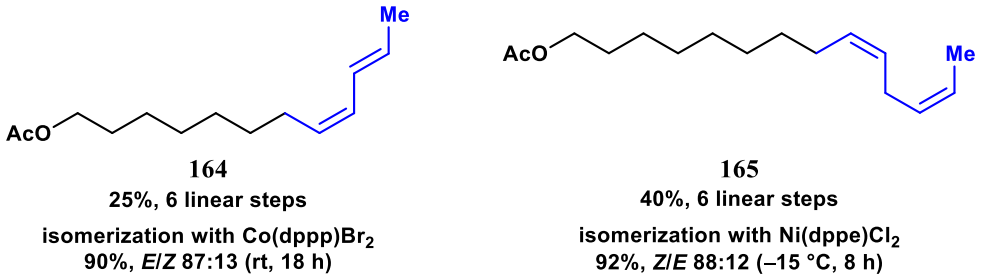


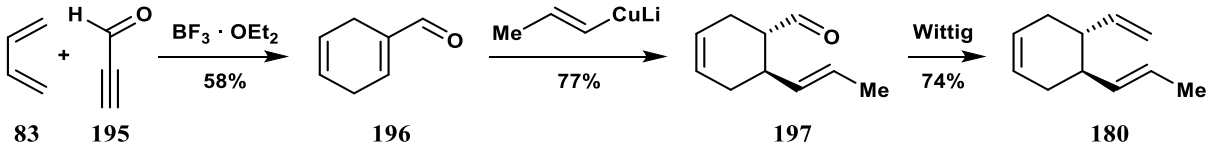
Figure 17: Accomplished total syntheses of C-12 pheromone **164** with 8*Z*,10*E*-diene substructure and C-14 pheromone **165** with 9*Z*,12*Z*-diene moiety.

Rolf Emmerich is thankfully acknowledged for his synthetic contribution. The synthesis of (9*Z*,12*Z*)-tetradeca-9,12-dien-1-yl acetate was published in 2015.[103]

3.1.4.3 Attempted Synthesis of Aucanthen

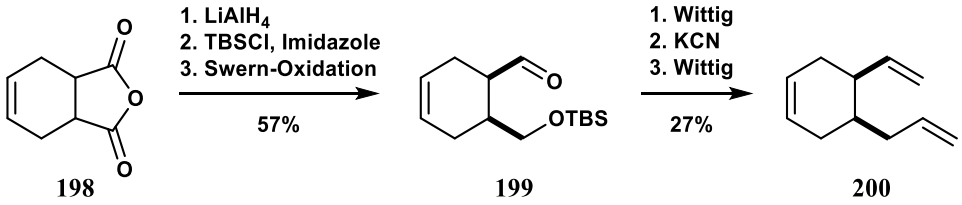
Besides the isomerization of the terminal double bond in presence of another internal double bond, the second challenge for the nickel-catalyzed isomerization would be an isomerization of a non-substituted terminal double bond, ideally to one single stereoisomer, in presence of another α-double bond with sterically more demanding substituents. This structure motif can be found in the natural product aucanthen (**180**), one of the ingredients of an odorous substance

of the marine brown alga *cutleria multifida*.[116] The hypernym "aucanthen" describes a whole family of stereoisomers and diastereomers with the skeletal backbone shown in Figure 14. Browne *et al*. addressed the *trans*-configured diastereomer of the molecule in a simple enantioselective three-step synthesis. The reaction is shown in Scheme 82.[120]



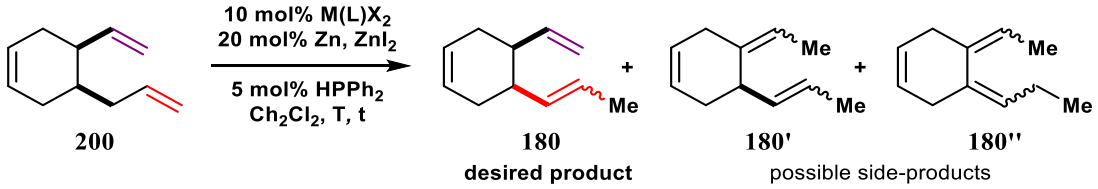
Scheme 82: Aucanthen synthesis by Browne *et al*.

The following approach started with a reduction of tetrahydroisobenzofuran-1,3-dione (**198**) and subsequent TBS-monoprotection and Swern oxidation to give aldehyde **199** in 57% over three linear steps. The associate test molecule with two terminal double bonds in close proximity, diene **200**, could be synthesized in another three steps with an overall yield of 27%. Philip Horx is thankfully acknowledged for his synthetic contribution towards the synthesis of **200**.



Scheme 83: Synthesis of the potential aucanthen precursor **200**.

The final isomerization key step was carried out under different conditions, which are summarized in Table 3.



Scheme 84: Isomerization of diene **200** to the desired aucanthen diastereomer **180** and probable side-products.

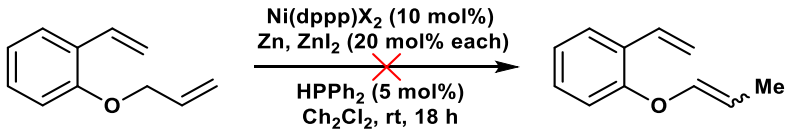
Unfortunately, a chemoselective isomerization of the allylic terminal double bond (highlighted in red in Scheme 84) next to the vinylic double bond (highlighted in purple) did not succeed. Only at ambient temperature, a reaction took place. A mixture of isomers was detected *via* GC/MS analysis, though. Probably, the vinylic double bond was also isomerized to the thermodynamically favored trisubstituted position as shown for compounds **180'** and **180''**.

Table 3: Attempts for the isomerization of diene **200**.

entry	M(L)X_2	*T* / *t*	reaction progress[a]
1	Ni(dppp)Cl_2	rt, 1 h	unselective reaction
2	Ni(dppp)Cl_2	–30 °C, 3 h	low conversion
3	Ni(dppp)Cl_2	–20 °C, 3 h → rt, o/n	low conversion, then unselective
4	Ni(dppp)Cl_2	0 °C, 18 h	low conversion
5	Ni(dppp)Cl_2 $HSiEt_3$[b]	–30 °C, 3 h	unselective reaction
6	Co(dppp)Br_2	rt, 18 h	no conversion

a: General reaction conditions: M(L)X_2 (10 mol%), Zn, ZnI_2 (20 mol%), $HPPh_2$ (5 mol%) in dichloromethane (0.1 M), 10 min stirring at rt, then addition of diene **200** (1.0 M) and stirring at rt for the desired time;
b: Triethylsilane (1.5 eq) was used instead of $HPPh_2$.

Nevertheless, the limitations of our catalyst system could be identified. Due to the close proximity of both terminal alkene moieties, a coordination of the catalyst to the two double bonds could be the reason that the reaction does not proceed at lower temperatures. The same result was observed, when trying to isomerize allylstyrylether **201**, as shown in Scheme 85.



201 **202**

Scheme 85: Attempted isomerization of allylether **201.**

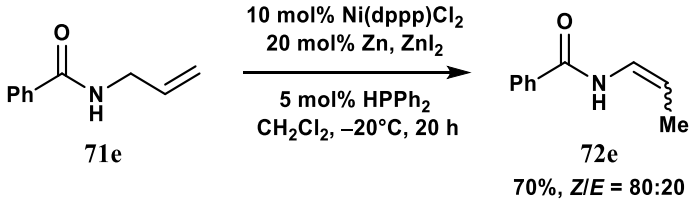
3.1.5 Isomerization of N-Allyl Amides and N/O-Allyl Carbamates

In constant search for higher functionalized substrates, Anastasia Schmidt already identified amines and amides as non-applicable susbtrates for the cobalt-catalyzed double bond transposition, since they led to a deactivation of the cobalt catalyst presumably due to coordination.[33] Other alumni of the Hilt group described the same observation when they applied starting materials with a free NH-group for a cobalt-catalyzed hydrovinylation reaction.[121] At that point, the nickel-based catalyst system could provide a remedy by enabling the isomerization of nitrogen-containing molecules. The substrate screening for the nickel-based catalyst system revealed that amines are no suitable substrates, either, as they lead to inhibition of the catalyst without any conversion occurring. As already described above, similar nickel catalysts have been applied for the isomerization of *N*-allyl amides and carbamates by Liu, Manolikakes, and Moran.[50–52] Liu and Manolikakes obtain a rather unselective *Z*/*E* mixture of the corresponding enamides and enecarbamates,[50,51] so that there is still a strong need for a *Z*-selective isomerization of *N*-allylic compounds. Helpful discussions with the latter led to the idea of testing the same substrate class for a regioselective double bond transposition with our nickel-based catalyst system.

The following chapters describe the results achieved towards the desired *Z*-selective isomerization of *N*-allyl amides and carbamates. The synthesis of the starting materials followed literature-known procedures[122] and can be found in the experimental section. The results were published in 2016.[123]

3.1.5.1 *Z*-Selective Isomerization of Secondary *N*-Allyl Amides and Carbamates

For an initial screening of reaction conditions, the established nickel catalyst system was applied according to a modified GP 1 (GP 2 in experimental section). Complete conversion of the test substrate *N*-allyl benzamide **71e** was achieved after 20 h stirring at –20 °C with an isolated yield of 70% and an acceptable *Z*/*E* ratio of 80:20.



Scheme 86: Isomerization of the test substrate *N*-allyl benzamide (**71e**).

The conversion of the starting material and the *Z*/*E* ratio were monitored by GC/MS analysis. The determination of the final *Z*/*E* ratio after purification was confirmed by NMR spectroscopy

and verified by GC/MS analysis. As already seen above for other substrates, the performance of the reaction at ambient temperature provided a diminished *Z*-selectivity. More precisely, the thermodynamic equilibration led to a *Z*/*E* ratio of 45:55 and an isolated yield of 83%. Since the yield of the resulting enamide **72e** was not yet adequate, a modification of the initial reaction conditions regarding the nature and amount of the Lewis acid, which could be the reason for a loss of yield, was addressed. The reactions were performed at –20 °C with a reaction time of 20 h (cf. Scheme 86) and 20 mol% Lewis acid, unless otherwise stated (Table 4, entry 6).

Table 4: Modifications of the reaction conditions by varying the amount and nature of the Lewis acid.

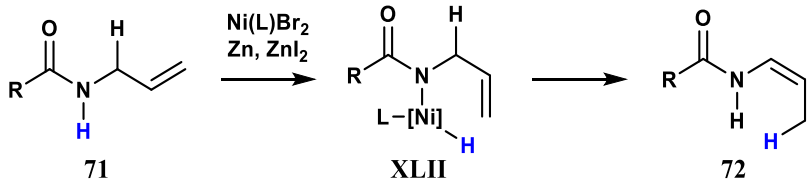
entry	Lewis acid	reaction	purification	*Z*/*E*	yield[a]
1	**ZnI_2**	**complete conversion**	**FC (Silica)**	**80:20**	**70%**
2	ZnI_2	complete conversion	FC (Silica, 1% NEt_3)	66:34	47%
3	10 mol% ZnI_2	85% conversion	FC (Silica)	67:33	62%
4	without ZnI_2	7% conversion	-	-	-
5	$ZnCl_2$	60 % conversion	FC (Silica)	74:26	55%
6	AgOTs	no conversion (–20 °C and rt, 48 h)	-	-	-
7	AgOAc	complete conversion (24 h)	FC (Silica)	65:35	71%
8	$BF_3 \cdot OEt_2$	no conversion	-	-	-
9	$TiCl_4$	decomposition of the s.m.	-	-	-

a: General reaction conditions: $Ni(dppp)Cl_2$ (10 mol%), Zn, ZnI_2 (20 mol%), $HPPh_2$ (5 mol%) in dichloromethane (0.1 M), 10 min stirring at rt, then addition of *N*-allyl benzamide (1.0 M) and stirring at –20 °C for 20 h, unless otherwise stated (s.m. = starting material).

The purification of enamide **72e** was performed *via* flash column chromatography on silica, making sure that both isomers (which sometimes varied in their R_f values on the TLC plate) were completely flushed down. Since a decomposition of the product can also occur on an acidic stationary phase, the silica was impregnated with 1 vol% triethylamine to prevent the product from potential decomposition (Table 4, entry 2). This led to a decrease in yield, so that silica was the stationary phase of choice. The amount and nature of the Lewis acid was further addressed. When only 10 mol% ZnI_2 under otherwise steady reaction conditions were used, incomplete conversion (85% after 20 h at –20 °C, entry 3) could be detected *via* GC/MS. In the

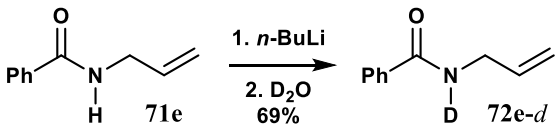
absence of ZnI_2 only 7% conversion were observed (entry 4). The Lewis acid was crucial for the activation of the catalyst. A halide substitution of ZnI_2 to $ZnCl_2$ (20 mol%) was possible, but a longer reaction time was necessary, due to incomplete conversion of the starting material (80% after 20 h at –20 °C). The use of other Lewis acids such as AgOTos (entry 6, no conversion) was also unsuccessful. The use of strong Lewis acids, such as $BF_3 \cdot Et_2O$, or $TiCl_4$ led to decomposition of the starting material. Alone, the application of AgOAc led to full conversion after 48 h. However, an inferior excess of the *Z*-isomer (*Z*/*E* = 65:35, entry 7) was formed. All Lewis acids led to comparable or lower isolated yields of the enamide than obtained with the use of 20 mol% ZnI_2, so that in conclusion ZnI_2 remained as the Lewis acid of choice.[123] Variation of the ligand revealed that dppp acts superior to dppe and other substituted dppp derivatives. Too bulky ligands, such as dpppBuEt or bdpp, led to a significant decrease in conversion of the starting material or completely shut down the reaction.

During her Master thesis, Corinna Kohlmeyer revealed that, similar to $HPPh_2$, other hydrogen sources, such as silanes, water, and even amines, were able to transfer the hydrogen to the substrate initiating an isomerization process. Unfortunately, the addition of other hydrogen sources always decreased the *Z*-isomeric excess in the product mixture. Kohlmeyer observed that the *Z*-isomer is transferred to the *E*-isomer even though a full conversion of the terminal alkene was not obtained. The amount of other internal isomers was increased when an amine is added.[112] On basis of these results, a potential involvement of the amidic hydrogen atom of **71** (highlighted in blue in Scheme 87) could be possible.



Scheme 87: Possible involvement of the secondary amide group in the catalytic cycle.

To test, if the hydrogen located at the nitrogen atom was somehow involved in the catalytic cycle, the *N*-deuterated benzamide derivative **72e**-*d* was synthesized.

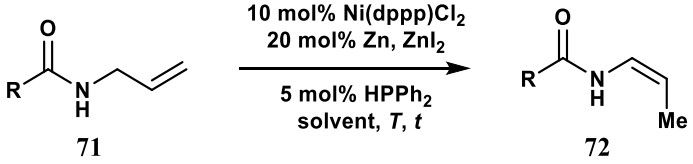


Scheme 88: Deuterium-labeling of *N*-allyl benzamide (**71e**).

No isomerization of the secondary amides took place in the absence of $HPPh_2$. Isomerizing the deuterated benzamide **72e**-*d* in presence of $HPPh_2$, the desired reaction occurred. In the product,

no deuterium could be detected *via* GC/MS analysis and ^{2}H NMR spectroscopy. In conclusion, the free NH-group did not participate in the catalytic cycle, since deuterium was not incorporated in the alkenyl chain of the isomerized product.

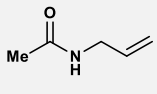
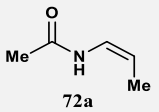
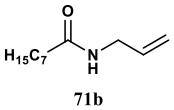
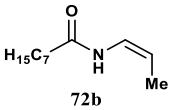
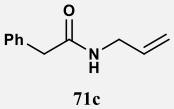
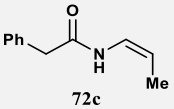
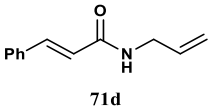
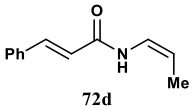
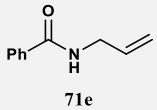
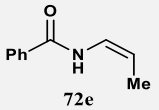
With the final reaction conditions in hand, the substrate screening was focused on temperature modifications to obtain the best possible *Z*-selectivity. Similar to the results in my Master thesis, a targeted adjustment of the reaction temperature is necessary for each substrate.[102]

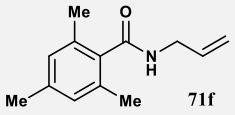
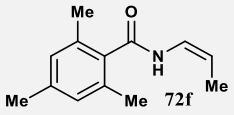
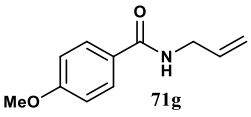
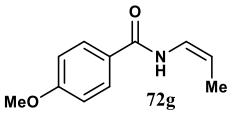
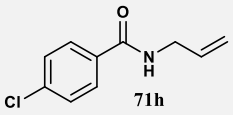
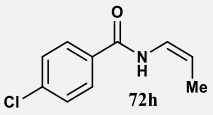
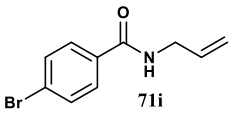
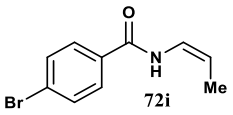
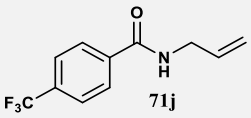
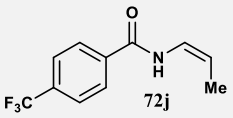
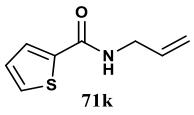
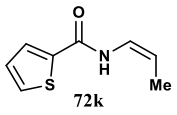


Scheme 89: Isomerization of secondary *N*-allyl amides.

A study was then carried out to screen a number of representative secondary *N*-allyl amides with different alkyl and aryl substituents and reaction temperatures. The reactions were performed in cooperation with Philipp Steinlandt in the course of his Bachelor thesis.[124] The best reaction conditions for each substrate, giving the highest conversion, the lowest amount of side products, and the best *Z*-isomeric excess, are summarized in Table 5.

Table 5: Substrate scope of the isomerization of secondary *N*-allyl amide of type **71**.

entry	starting material	main product	*T*, *t*	yield	*Z*/*E* ratio[a]
1	 71a	 72a	–20 °C, 48 h	12%	80:20
2	 71b	 72b	RT, 90 min	42%	82:18
3	 71c	 72c	–30 °C, 64 h	60%	92:8
4	 71d	 72d	83 °C,[b] 144 h	54%	50:50
5	 71e	 72e	–30 °C, 64 h	74%	91:9

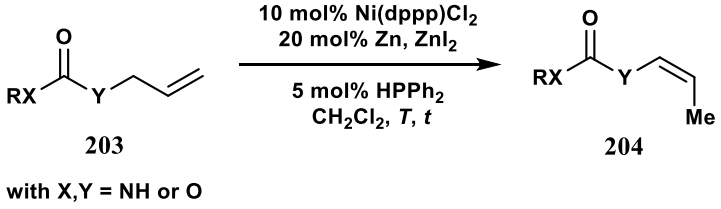
entry	starting material	main product	*T*, *t*	yield	*Z*/*E* ratio[a]
6	 71f	 72f	rt, 168 h[c]	47%	86:14[d]
7	 71g	 72g	rt, 192 h[c]	70%	64:36
8	 71h	 72h	–20 °C, 39 h	66%	81:19
9	 71i	 72i	–25 °C, 69 h	62%	93:7
10	 71j	 72j	18 °C, 45 h	63%	78:22
11	 71k	 72k	5 °C, 72 h	33%	84:16

a: General conditions: $Ni(dppp)Cl_2$ (10 mol%), Zn, ZnI_2 (20 mol% each), $HPPh_2$ (5 mol%) in dichloromethane (0.1 M), stirring for 10 min at rt and then cooling to desired temperature. Addition of 1.0 eq *N*-allyl amide; b: The reaction was performed in acetonitrile (1.0 M) instead of dichloromethane; c: Additional catalyst was added, see experimental section; d: A rotameric mixture of the product was obtained, see experimental section (the *Z*/*E*/s.m. ratio is 79:10:11).

The use of the simplest alkyl chain R = Me resulted in isolation issues of the product **72a**. Because of the product's high volatility, the solvent could not be removed completely, and the yield was extremely low (Table 5, entry 1). The isomerization of *N*-allylacetamide (**71a**) gave a good *Z*/*E* ratio of 80:20. The introduction of a longer aliphatic side chain **72b** solved the isolation issue. The yield remained relatively low (42%) and the reaction temperature had to be raised to ambient temperature to guarantee a satisfying conversion of the starting material **71b** with a comparable *Z*/*E* ratio of 82:18. In general, aromatic amides **71c,h,i** were more reactive. The isomerization could be performed at lower temperatures with better *Z*/*E* ratios. The benzylic amide **71c** could be isomerized at –30 °C to furnish the product **72c** in acceptable yield (60%) and good stereoselectivity with an isomeric excess (*ie*) of 84% (Table 5, entry 3). Of similar high reactivity was the benzamide derivative **71e** (Scheme 86), which led to the formation of enamide **72e** in slightly better yield and *Z*/*E* ratio (74%, *Z*/*E* = 91:9, entry 5). On

the other hand, the substrates derived from cinnamamide (**71d**), the sterically hindered mesityl-substituted amide **71f**, and 4-methoxyphenyl-*N*-allylamide (**71g**) required prolonged reaction times and elevated temperatures (83 °C), so that the reaction had to be performed in acetonitrile instead of dichloromethane. In general, the latter gives the best isomeric excesses of *Z*/*E* 64:36 (entry 7) for these electron-rich substrates. The addition of more catalyst was necessary to obtain full conversion of the *N*-allyl amides **71f** and **71g**. Electron-withdrawing substituents on the arene moiety, such as halide- and trifluoromethyl-substituted benzamides **71h,i** and **71j** were more reactive and resulted in isomeric excesses of up to 86% (entry, 9). The idea that a weak coordination site, such as the thiophene substituent, would be beneficial (**71k**), could not be established. The isomerization of **71k** gave an acceptable *Z*/*E* ratio (84:16), but poor yield (33%, entry 11).[123]

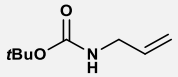
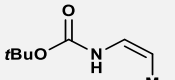
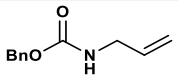
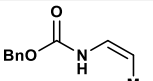
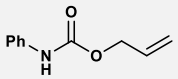
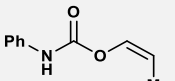
The suitability of *N*-allyl carbamate derivatives as an alternative functional group was further investigated, as Scheme 90 depicts.



Scheme 90: Isomerization of secondary *N*-allyl carbamates.

Initial screening started with the Boc-protected allylamine **203a** leading to the same results as above. The best *Z*-isomeric excess of 62% (*Z*/*E* = 81:19) was obtained at −30 °C after 19 h reaction time (Table 6, entry 1). Performance of the isomerization at ambient temperature led, again, to a decrease of the *ie* (44% of *Z*-isomer). Although the reactivity of all substrates was sufficient and moderate to acceptable yields of up to 79% could be realized, the *Z*/*E* ratios of the products **204b** and **204c** were inferior to the previously reported benzamide derivatives **72**. Furthermore, enecarbamate **204c** was sensitive towards the reaction conditions and the Lewis acid was found to cause the formation of decomposition products, such as benzylic alcohol (in the case of enecarbamate **204b**, as well as phenyl isocyanate and aniline for **204c** (entry 3), which explains the moderate yield of **204c**.

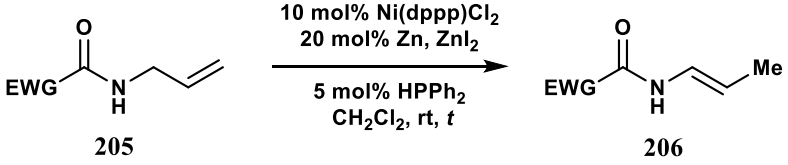
Table 6: *Z*-Selective isomerization of selected secondary *N*-allyl carbamates.

entry	starting material	main product	*T*, *t*	yield	*Z*/*E* ratio[a]
1	 203a	 204a	–30 °C, 19 h	79%	81:19
2	 203b	 204b	–30 °C, 17 h	69%[b]	81:19
3	 203c	 204c	–20 °C, 48 h	36%[c]	87:13

a: General conditions: $Ni(dppp)Cl_2$ (10 mol%), Zn, ZnI_2 (20 mol% each), $HPPh_2$ (5 mol%) in dichloromethane (0.1 M), stirring for 10 min at rt and then cooling to desired temperature. Addition of 1.0 eq allyl carbamate. b: Benzylic alcohol as side product was detected *via* GC/MS analysis; c: Phenylisocyanate and aniline were detected *via* GC/MS analysis.

3.1.5.2 *E*-Selective Isomerization of Electron-Deficient *N*-Allyl Amides

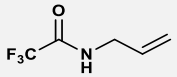
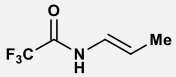
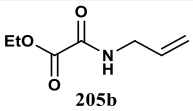
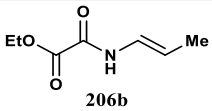
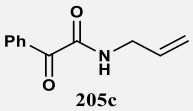
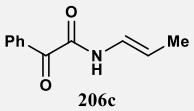
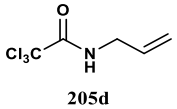
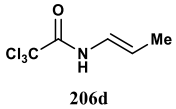
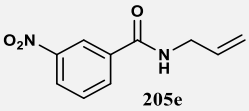
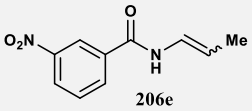
Interestingly, the use of secondary electron-deficient *N*-allyl amides resulted in the formation of the *E*-isomer **206** as the major product.[123] The same results were observed, when electron-deficient α-keto *N*-allyl amides were used.



Scheme 91: Isomerization of electron-deficient *N*-allyl amides (EWG = electron withdrawing group)

Table 7 gives an overview. Unfortunately, allyl amide **205d** with an attached trichloromethyl group could not be transferred to the corresponding enamide (entry 4), maybe due to steric hindrance. The isomerizations had to be performed at ambient temperature, otherwise the reactions did not proceed (entries 1-3).

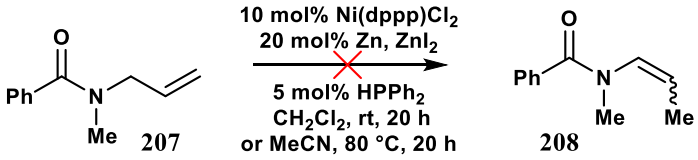
Table 7: Isomerization of electron-deficient substrates.

entry	starting material	main product	*T*, *t*	yield	*Z*/*E* ratio[a]
1	 **205a**	 **206a**	rt, 64 h	64%	15:85
2	 **205b**	 **206b**	rt, 95 h	29%	8:92
3	 **205c**	 **206c**	rt, 48 h	n.i.[b]	*E* only
4	 **205d**	 **206d**	rt, 72 h	no reaction	-
5	 **205e**	 **206e**	rt, 24 h	no reaction	-

a: General conditions: $Ni(dppp)Cl_2$ (10 mol%), Zn, ZnI_2 (20 mol% each), $HPPh_2$ (5 mol%) in dichloromethane (0.1 M), stirring for 10 min at rt. Addition of 1.0 eq allyl amide and stirring at rt for the desired time; b: n.i. = not isolated. *Z*/*E* ratio was determined *via* GC/MS analysis.

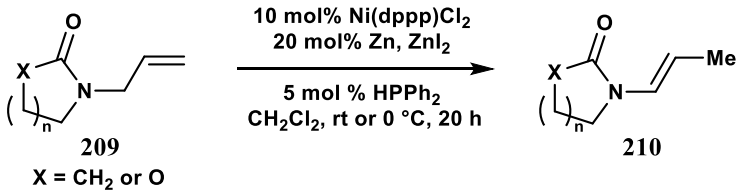
3.1.5.3 *E*-Selective Isomerization of Tertiary *N*-Allyl Amides

Besides the isomerization of secondary allylic amides, the question arised, if it is also possible to isomerize sterically more hindered *N*-alkylated derivatives. Unfortunately, even at elevated reaction temperatures *N*-methylated amide **207** gave no conversion at all, maybe due to steric hindrance.



Scheme 92: Isomerization of *N*-allyl amide **207**.

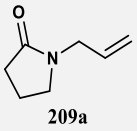
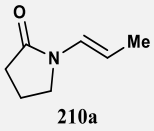
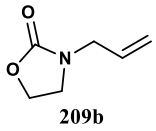
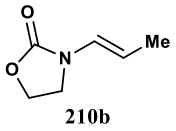
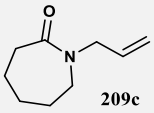
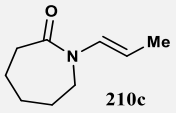
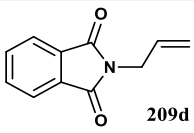
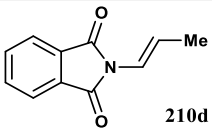
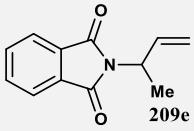
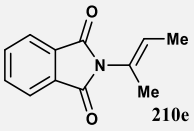
Changing the methyl group to a rotationally more flexible *n*-butyl rest, the reaction did not proceed, either. Consequently, the question arised, if a free NH-group is beneficial for the nickel-catalyzed translocation of double bonds.[123] Therefore, other cyclic tertiary *N*-allyl derivatives (Scheme 93) were investigated in cooperation with Monika Ballmann.



Scheme 93: Isomerization of tertiary *N*-allyl lactams and oxazolidinones.

The results of the nickel-catalyzed reactions are summarized in Table 8.

Table 8: Scope of the isomerization of tertiary *N*-allyl lactams and oxazolidinone of type **209**.

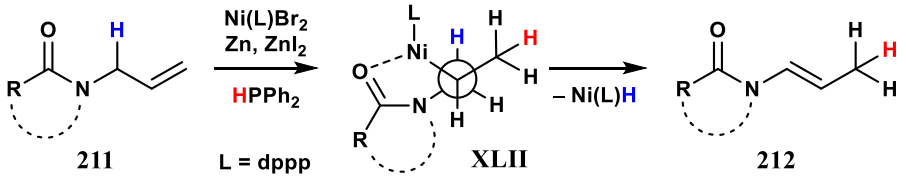
entry	starting material	main product	*T*, *t*	yield	*Z*/*E* ratio
1	 209a	 210a	rt, 24 h	98%	*E* only
2	 209b	 210b	rt, 16 h	93%	6:94
3	 209c	 210c	rt, 18 h	77%	*E* only
4	 209d	 210d	rt, 18 h[b]	85%	*E* only
5	 209e	 210e	0 °C, 72 h	70%	33:67

a: General conditions: Ni(dppp)Cl_2 (10 mol%), Zn, ZnI_2 (20 mol% each), $HPPh_2$ (5 mol%) in dichloromethane (0.1 M), stirring for 10 min at rt and then cooling to desired temperature. Addition of 1.0 eq *N*-allyl lactam; b: Ni(dppp)Br_2 was used instead of Ni(dppp)Cl_2.

N-allyl lactam systems were also isomerizable giving selectively the *E*-configured enamides in good yields. Simple lactams (**209a**/**209c**) or *N*-allyl phthalimide (**209d**) gave exclusively the *E*-isomer at ambient temperatures . The *E*-selectivity of oxazolidinone **209b** (*Z*/*E* = 6:94, Table 8, entry 2) was somewhat lower compared to the lactams. In case of the isomerization of branched systems, the racemic substrate **209e** was applied. The desired product **210e** was obtained as a 33:67 mixture of *Z*- and *E*-isomer with a prolonged reaction time of 72 h (entry 5).

Nevertheless, cyclic amides gave the *E*-configured products in outstanding yield and selectivity. A possible steric hindrance of the cyclic structure furnished the observed *E*-configuration of the

product. In contrast, the isomerization of the corresponding *N*-methyl derivative **207** failed. An interesting finding might be rationalized by the conformation the substrate adopts when coordinating to the nickel-catalyst during the overall 1,3-hydrogen shift process. According to the work of Hesse[49] concerning his iron catalyst this conformation could be explained and adopted for the nickel catalyst. A *cis*-elimination of the nickel hydride is only possible from the sterically not hindered intermediate **XLII**, where the carbonyl group coordinates to the nickel catalyst (cf. Scheme 94). A *Z*/*E* ratio of 0:100 is unlikely a thermodynamically equilibrated process.[123]



Scheme 94: Possible explanation for the stereochemical outcome.

Besides the tertiary *N*-methylated amide **207** other substrates were found, which were not applicable, since potential coordination to the catalyst could inhibit the reaction. Non-cyclic tertiary amides as well as sulfonamide **214**, Weinreb amide **215**, and urea derivative **216**, shown in Figure 18, did not undergo the desired isomerization process.

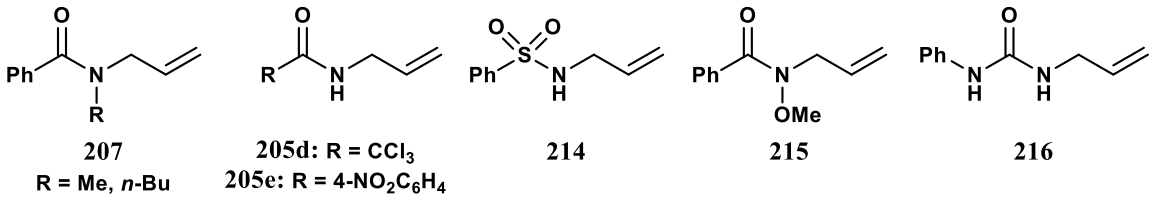
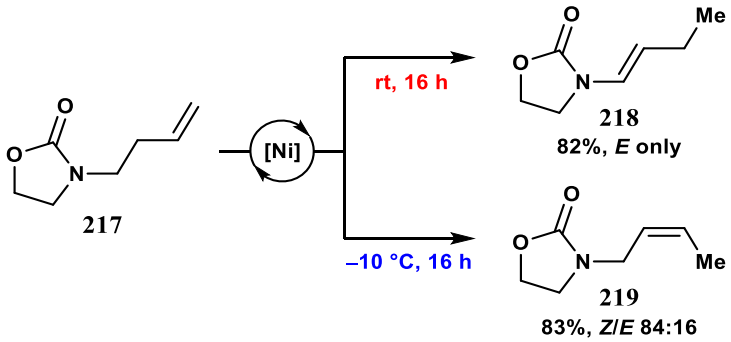


Figure 18: Substrates, which gave no conversion.

Finally, the double bond transposition was realized along a longer alkyl chain by a targeted adjustment of the reaction temperature to differentiate between a single and a twofold translocation process. *N*-Homoallyl oxazolidinone **217** was applied to the nickel catalyst system at different temperatures. The best results with respect to selectivity and yield are shown in Scheme 95.[123]



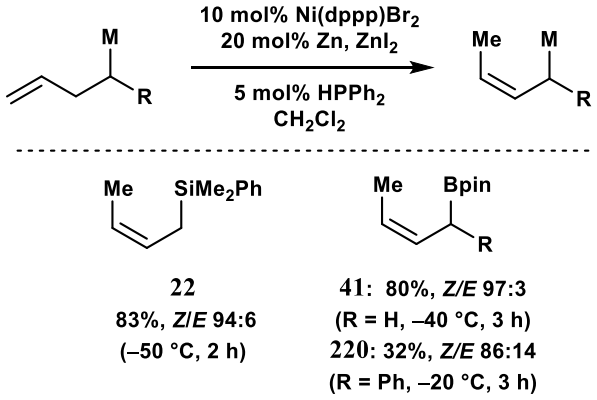
Scheme 95: Temperature-dependent isomerization of *N*-homoallyl oxazolidinone **217**.

As already observed during the isomerization of more simple functionalized substrates,[103] the adjustment of the reaction temperature can conveniently direct the nickel-catalyzed transposition of the terminal double bond towards the *Z*-selective migration over one single position obtaining allyl carbamate **219** in 83% yield and a *Z*/*E* ratio of 84:16. At –10 °C the maximum achievable conversion of the starting material was 88%. When the reaction temperature was raised to ambient temperature two 1,3-hydrogen shifts occurred and the transposition proceeded towards the thermodynamically favored product, enamide **218**, in an *E*-selective reaction and a good yield of 82%.[123]

In summary, the nickel-based catalyst system bearing $HPPh_2$ as co-ligand was able to isomerize the terminal double bond in secondary *N*-allylic amides and carbamates towards *Z*-configured enamides and enecarbamates. The NH-group does not participate in the reaction. In *N*-allyl lactams and oxazolidinones, the nickel catalyst led to the translocation of the double bond with outstanding *E*-selectivity. Furthermore, a temperature-controlled single or double migration process could be realized to either generate the *Z*-configured allyl amide **219** or the *E*-configured enamide **218** (scheme 25).

3.2 Nickel-Catalyzed Diastereoselective Isomerization/Allylboration Sequence

Homoallylic boronic esters and silanes could successfully be isomerized to their corresponding *Z*-configured crotyl derivatives with the established nickel catalyst according to GP 1. Scheme 96 shows the substrates, which were accessible during the substrate screening.[102]

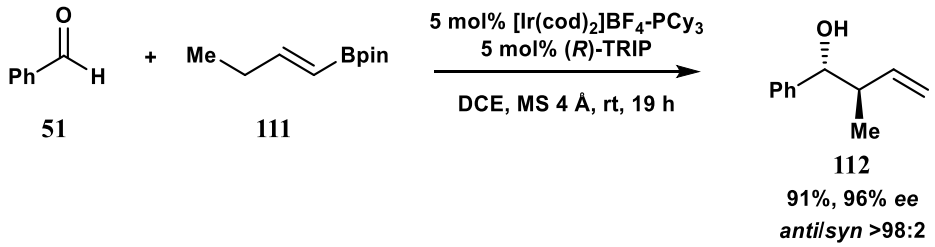


Scheme 96: *Z*-selective isomerization of homoallyl boronic esters and silanes.

Crotyl pinacol boronates **41** and **220** gave excellent *Z*-selectivities of up to 97:3 without the formation of the corresponding vinylboron product at low temperatures (–20 °C or –40 °C). The same phenomenon was observed when homoallyl silicon derivative **22** was used (*Z*/*E* 94:6 at –50 °C).[102]

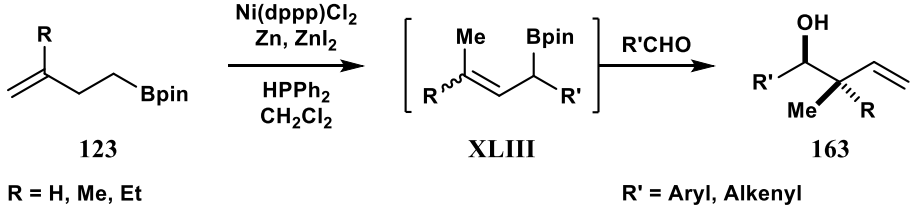
The resulting crotyl boron and silicon species should be perfectly qualified for a combination of the nickel-catalyzed isomerization step with a subsequent carbonyl allylation reaction. With regards to a synthetically useful one-pot transformation, the catalyst should generate a high *Z*-selectivity in presence of an aldehyde. The isomerization should not proceed faster than the allylboration step to decrease the number of other isomers formed in the process. The allylboration must proceed diastereoselectively to transfer the stereochemical information of the crotyl species into the product, anticipating the allylboration to proceed through a six-membered Zimmerman-Traxler transition state.

The isomerization itself can take place in two different directions. As Murakami has shown in 2013, the double bond could either isomerize away from the boronic ester function to form *E*-selectively a crotyl boronic acid pinacol ester from vinyl boronate **111** *via* iridium-catalysis (Scheme 97).[75]



Scheme 97: Diastereo- and enantioselective isomerization/allylboration sequence by Murakami *et al*.

In this chapter, the complementary isomerization to the *Z*-configured crotyl boronic ester starting from homoallylic boronic esters of type **123** is described. Following the original protocol for the *Z*-selective olefin isomerization, the double bond migrates towards the functional group as Scheme 98 depicts.[103] In presence of an aldehyde R'CHO, the isomerization is automatically stopped by the allylboration at the point where the double bond is located in the allylic position (compound **XLIII**) resulting in the diastereoselective formation of homoallylic alcohols **163** with two adjacent stereocenters.

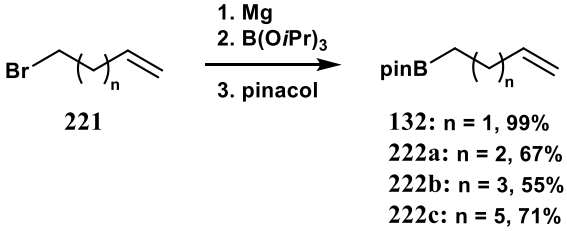


Scheme 98: Desired transformation of homoallylboron species **123** to *syn*-configured homoallyl alcohols **163**.

The results described below were published in 2016.[125] Monika Ballmann, Corinna Kohlmeyer, Sebastian Brunen and Luca Schmermund are thankfully acknowledged for their synthetic contribution.

3.2.1 Synthesis of the Boronic Esters

In order to achieve the desired one-pot sequence, a series of boronic esters was prepared first. Unsubstituted alkenyl boronic esters could be synthesized according to a procedure by Hilt[79] by Grignard reaction from bromide **221** providing unsaturated products **132** and **222a-c** with different alkenyl chain lengths in up to 99% yield.



scheme 99: Grignard reaction to the desired alkenyl pinacol boronates.

For a future variation of the allylation product's substitution pattern (cf. compound **123** in Scheme 98), differently substituted homoallyl boronic acid pinacol esters were further synthesized. An overview is shown in Figure 19.

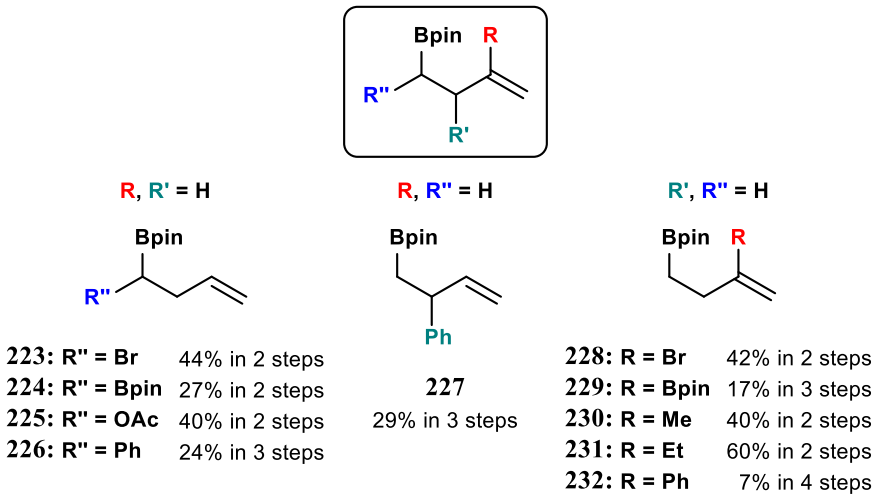
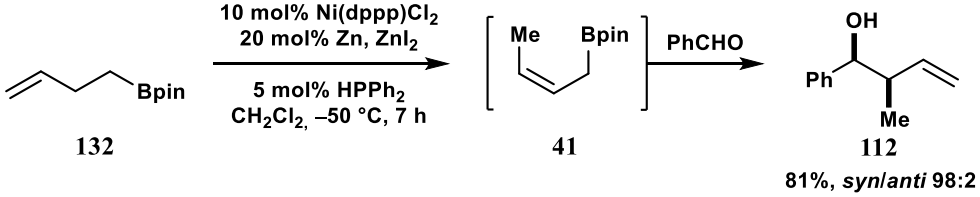


Figure 19: Substituted homoallyl boronates for the desired one-pot isomerization/allylboration sequence.

Usually, the boronic esters were synthesized according to literature-known procedures. Further information and references can be found in the experimental section.

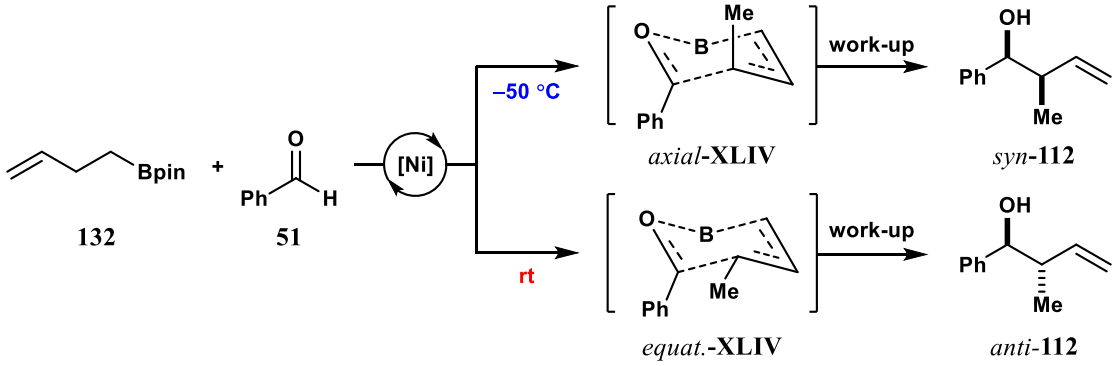
3.2.2 syn-Selective Isomerization/Allylboration Sequence of Unsubstituted Homoallyl Boronic Esters

Initial results concerning the functional group tolerance of the catalyst exposed that when benzaldehyde is added to the isomerization of homoallyl boronic acid pinacol ester (**132**) in the presence of the nickel catalyst system, the corresponding *syn*-configured allylboration product **112** could be obtained in a diastereomeric ratio (*d.r.*) *syn*/*anti* of 80:20 at –30 °C. Lowering the temperature to –50 °C, the desired homoallyl alcohol **112** could be isolated in 81% yield and excellent *d.r. syn*/*anti* of 98:2 (Scheme 100). The reaction could also be accomplished in the absence of zinc iodide, but in this case the conversion of the starting material was way lower. Again, $HPPh_2$ is inevitable for the reaction.



Scheme 100: Isomerization of homoallyl pinacol boronic ester **132** and subsequent allylboration of benzaldehyde.

When the reaction sequence was performed at ambient temperature, an additional transposition toward vinyl pinacol boronic ester can be observed (~14%) indicating that a fast isomerization outruns the allylboration reaction at elevated temperatures.[126] The product **112** was obtained in moderate yield (27%), but lower diastereoselectivity (*syn*/*anti* = 80:20). The fact, that the *syn*-configured diastereomer **112** was formed as main diastereomer even at elevated temperature, led to the assumption that the *Z*-configured crotyl boronic ester is formed first, even though in somewhat inferior amount compared with the reaction at –50 °C. The subsequent allylboration was faster than the *Z* to *E*-isomerization of the double bond. With increasing reaction time, the reaction equilibrated forming a mixture of *syn*/*anti*-configured alcohol **112** as well as the vinyl boron species as minor products. However, transposition of **112** toward a corresponding allylic alcohol was not observed.[112] In general, an allylboration proceeds through a six-membered Zimmerman-Traxler transition state **XLIV** (Scheme 101). Since a predictable stereodifferentiation is required in the transition state, it can be assumed, that the *syn*-configured diastereomer was formed due to the *Z*-selectivity of the previous isomerization step. The *anti*-diastereomer was formed vice versa.[127] As Hoffmann *et al*. already explained in the 1980's, the formation of the Zimmerman-Traxler transition state is the rate-determining step of an allylboration reaction. In case of the *Z*-configured crotyl boronic ester, the methyl group in the transition state **XLIV** is located in an axial position. The *E*-isomer, with the methyl group being located equatorially, is the thermodynamic favored conformation. Besides steric demand, the thermodynamic stability of the transition state is driven by polar effects.[128] The pathway depicted in Scheme 101 can be assumed as the origin of the diastereoselectivity.



Scheme 101: *Z*/*E*-Selectivity of the isomerization as origin of diastereoselectivity (*equat*. = equatorial).

As mentioned above, the *syn*-configured diastereomer **112** was generated predominantly in the reaction sequence, thus the double bond transposition proceeded in a highly *Z*-selective fashion at low temperatures under kinetic control in the presence of benzaldehyde, which obviously did not inhibit the isomerization reaction. As Szabo described for a similar reaction, the regio- and

stereochemical integrity of allylboronate species can even be maintained at elevated temperatures.[127] The double bond should be configurationally stable in the subsequent allylboration. At ambient temperature, more *anti*-diastereomer is observed, leading to the conclusion that, after isomerization, the *E*-configured crotyl boronic ester is formed in a higher amount. Figure 20 illustrates the temperature-dependence of the one-pot isomerization/allylboration sequence using the example 2-methyl-1-phenylbut-3-en-1-ol (**112**).

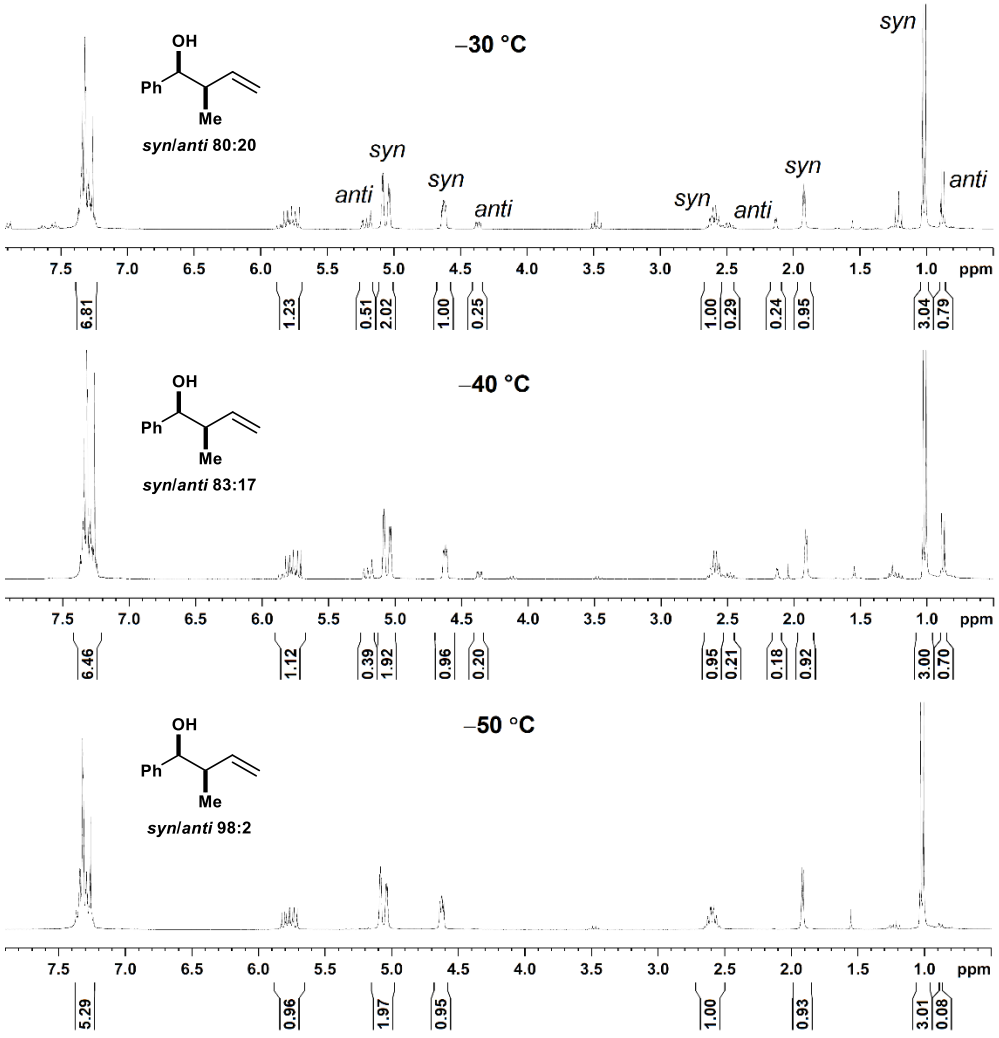
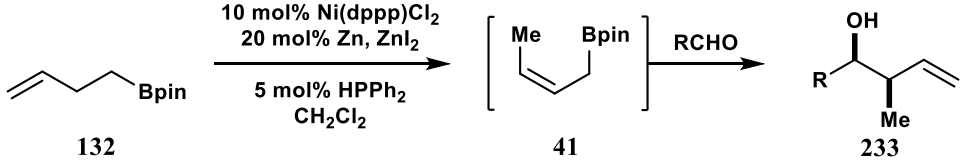


Figure 20: Temperature-dependence of the isomerization/allylboration sequence.

At –30 °C a *syn*/*anti*-ratio of 80:20 was obtained, which could be improved of up to 98:2 by lowering the temperature to –50 °C. The low temperature also prohibited the homoallylic alcohol **112** from isomerizing to the corresponding allyl alcohol. Further, compounds with a free hydroxyl group were no suitable substrates for the nickel-catalyst isomerization.[102] Only the cobalt catalyst tolerated unprotected hydroxyl groups.[32,33] For the diastereoselective allylboration sequence, the cobalt catalyst system was too unreactive, though.

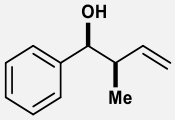
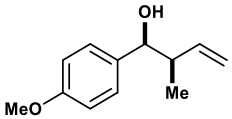
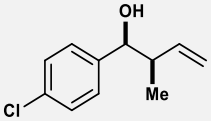
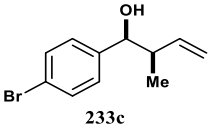
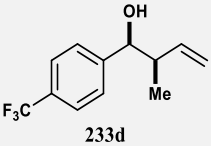
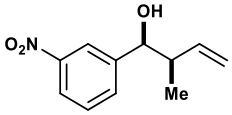
Based on these results, a number of functionalized aldehydes together with homoallylic boronic ester **132** were investigated in order to identify the scope and limitations of the nickel-catalyzed double bond transposition/allylation process. The reaction temperature and time have to be adjusted for each substrate combination.

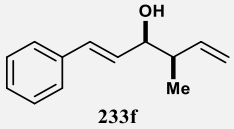
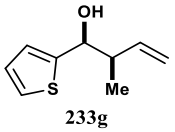
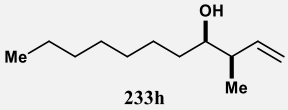


scheme 102: Isomerization of homoallyl pinacol boronic ester **132** and subsequent allylboration of different aldehydes.

The results are summarized in Table 9.

Table 9: Isomerization/allylboration of homoallyl boronic ester **132** with different aldehydes.

entry	main diastereomer	*T, t*	yield	*syn*/*anti* [a]
1	 **112**	–50 °C, 7 h	81%	98:2
2	 **233a**	–50 °C, 5 h	81%	96:4
3	 **233b**	–40 °C, 1 h	98%	97:3
4	 **233c**	–50 °C, 5.5 h	77%	97:3
5	 **233d**	–40 °C, 7 h	76%	95:5
6	 **233e**	–40 °C, 7 h	61%	98:2

entry	main diastereomer	*T, t*	yield	*syn*/*anti* [a]
7	 **233f**	–40 °C, 6 h	96%	92:8
8	 **233g**	–50 °C, 2 h	56%	86:14
9	 **233h**	–50 °C, 5 h	78%	95:5

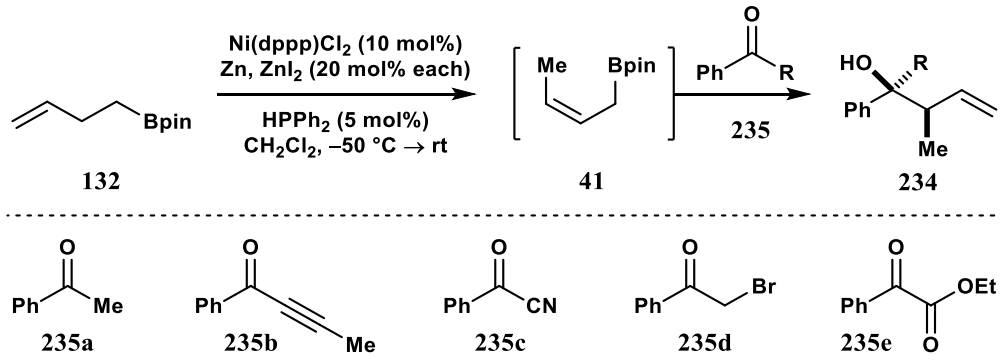
a: General conditions: $Ni(dppp)Cl_2$ (10 mol%), Zn, ZnI_2 (20 mol% each), $HPPh_2$ (5 mol%), 1.0 eq homoallyl boronic ester **132**, 1.0 eq aldehyde in dichloromethane (1.0 M). different reaction temperatures and times are listed above. The reaction temperature was adjusted with an acetone or isopropanol/dry ice bath.

In the GC/MS spectra, the peaks of the two diastereomers are merely baseline separated. Because of that, the *syn*/*anti* diastereomeric ratio was determined by ^{1}H NMR spectroscopy and compared to literature-known data. Functional groups, such as a methoxy group (**233a**, Table 9, entry 2), halides (**233b**, **233c**, entries 3-4), a trifluoromethyl group (**233d**, entry 5), and a nitro substituent on the phenyl ring (**233e**, entry 6) were well accepted and did not interfere with the catalytic system. Heterocycles, such as thiophene (**233g**) and *α*,*β*-unsaturated aldehydes (**233f**), were tolerated, as well. All products were obtained in good isolated yields and high diastereoselectivity (up to 98:2). Only the product derived from thiophene-2-carbaldehyde (**233f**) led to a lower yield of 56% and somewhat inferior diastereoselectivity of 86:14 (entry 8). Aliphatic aldehyde octanal led to the desired product **233h**, which was isolated in a good yield of 78% (entry 9). However, the determination of the diastereoselectivity of the overall process was problematic, since diagnostic ^{1}H NMR signals overlapped significantly. Nevertheless, the diastereoselectivity for the formation of **233h** could be estimated to be ~95:5 (GC/MS analysis). No other side products generated by follow-up transposition reactions were detected when the reaction sequence ran at low temperatures.[125]

3.2.2.1 Attempted Isomerization/Allylboration Sequence of Unsubstituted Homoallyl Esters with Activated Ketones

The isomerization/allyboration sequence with a broad scope of functionalized aliphatic and aromatic aldehydes gives the desired homoallylic alcohols **233** in high yield and excellent diastereomeric excess (*de*) of up to 96% *syn*-diastereomer. These results beg the question

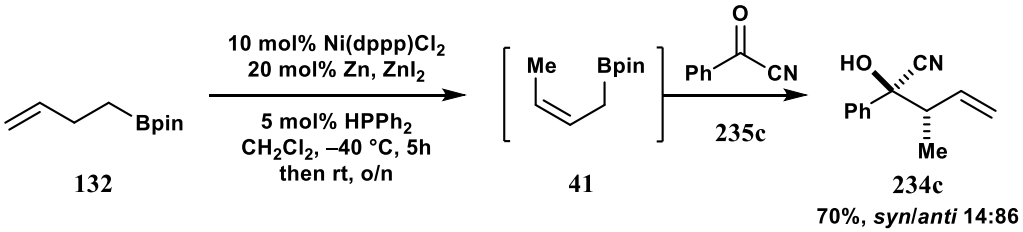
whether the method is also applicable for ketones, which would have higher steric demand and would therefore react slower compared to aldehydes. For a deeper investigation, a variation of activated ketones was selected, with the intention that they would be sufficiently reactive in the desired allylboration even in the absence of higher amount of an external Lewis acid. The reaction and the selection of ketones is illustrated in Scheme 103.



Scheme 103: Isomerization/allylboration sequence with activated ketones.

First, the isomerization reaction was performed at −50 °C ensuring a high *Z*-selectivity of the outcoming double bond in allylic position (compound **41**). Then, 1.0 equivalent (eq) of the ketone **235** was added and the mixture was stirred at ambient temperature overnight.

Unfortunately, the method did not work for the simple ketone acetophenone (**235a**) and neither for other electron-deficient ketones, such as alkynylketone **235b**, bromoacetophenone **235d**, or α-ketoester **235e** at different reaction temperatures. Alone, benzoyl cyanide (**235c**) was surprisingly able to undergo the desired transformation at ambient temperature leading to cyanhydrine **234c** in a *syn*/*anti*-ratio of 14:86 and 70% isolated yield. The product did not decompose to the corresponding ketone and was even stable on the acidic stationary silica gel phase during FC. The *anti*-diastereomer was the main product and was compared to appropriate literature.[127] At lower temperatures the ketone was not reactive enough.



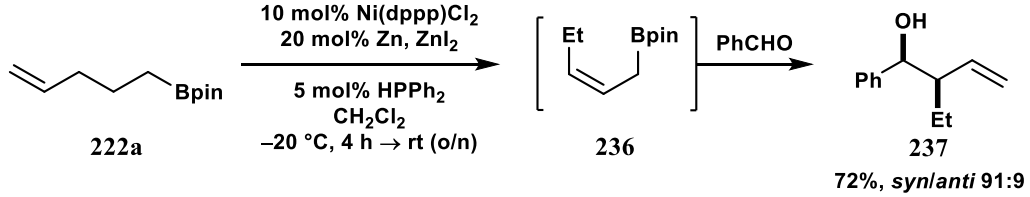
Scheme 104: *anti*-Selective isomerization/allylboration of homoallyl boronic acid pinacol ester **132** and benzoyl cyanide.

At this point, the allylboration of ketones can be assumed as a limitation. Probably due to steric hindrance, ketones are not reactive enough under the established reaction conditions.

Consequently, aldehydes were considered as the carbonyl moiety of choice for the rest of the reactions.

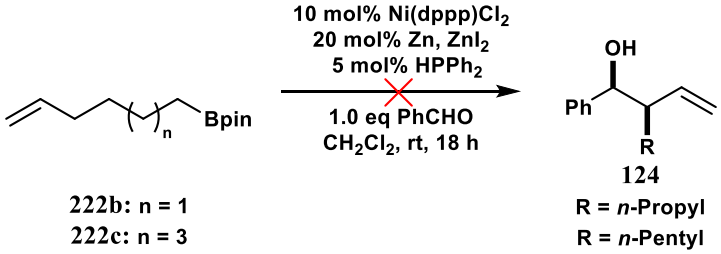
3.2.3 *syn*-Selective Isomerization/Allylboration Sequence of Long-Chain Alkenyl Boronic Esters

If chain walking of the metal hydride occurs, the double bond transposition could be realized along a longer carbon chain. This would allow the introduction of alkyl substituents other than a simple methyl group adjacent to the hydroxyl group in the product. As prototype substrate, 1-pentenyl pinacol boronic ester **222a** was reacted with the nickel catalyst system in the absence of benzaldehyde at low temperature (−20 °C), and a mixture of homoallyl and allyl pinacol boronates were detected. In the presence of benzaldehyde, even at temperatures as low as −20 °C, the double bond transposition proceeded twice, and the desired product **237** could be obtained in quite good yield of 72% and diastereoselectivity (*syn*/*anti* = 91:9).[125]



Scheme 105: Twofold double bond isomerization and subsequent allylboration of 1-pentenyl boronic acid pinacol ester and benzaldehyde.

When 1-hexenyl or 1-octenyl boronic esters **222b** and **222c** were applied, the isomerization yielded in an unselective mixture of internal isomers at different reaction temperatures, which did not undergo the desired allylboration (Scheme 106).

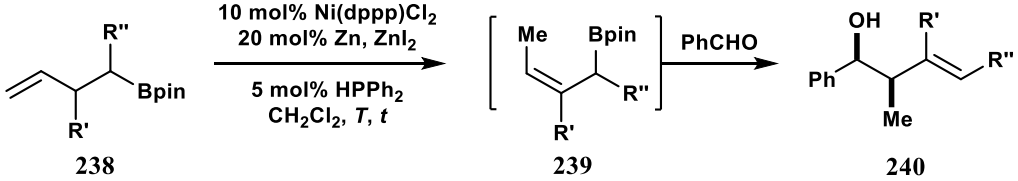


Scheme 106: Unsuccessful isomerization/allylboration of hexenyl- and octenyl boronic esters.

A controllable *Z*-selective isomerization *via* chain walking was therefore limited to two positions, otherwise a product mixture of internal isomers of the corresponding boronic ester was obtained. Since the double bond did not migrate right up to the necessary allylic position, a subsequent allylboration did not take place.

3.2.4 Isomerization/Allylboration Sequence of α- & β-Substituted Homoallyl Boronic Esters

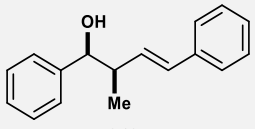
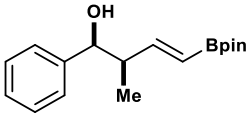
When the one-pot sequence was transferred to differently substituted boronic esters **238**, several substitution patterns in the desired homoallylic alcohol were addressable. The choice for the phenyl substituent at the α-carbon (**238** with R' = H, R'' = Ph in Figure 19) was rationalized by the expectation that the phenyl substituent would preferentially adopt an *E*-configuration in the corresponding product **240** in order to minimize the number of stereoisomers formed in the reaction sequence.[125]

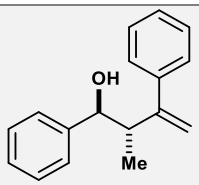
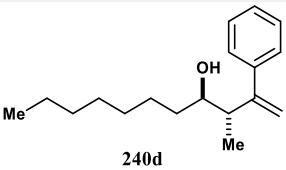


Scheme 107: Isomerization/allylboration of either α- or β-substituted homoallyl boronic esters.

A phenyl substituent in β-position (R' = Ph, R'' = H, entries 3 and 4) gave alcohol **240c** and **240d** in >99:1 *anti*-configuration (Table 10, entries 3 and 4). The phenyl substituent in this position hindered an isomerization at low temperatures. Full conversion of the starting material could be obtained at ambient temperature only, independent on the aldehyde used (entries 3 and 4 in Table 10).Vinyl boronate **240b** (R' = H, R'' = Bpin, entry 2) could be a potential nucleophile for a subsequent Suzuki cross-coupling reaction, since the second Bpin-moiety remains intact after the first allylboration. The product is formed in 71% with a diastereomeric excess (*de*) of the *syn*-configured product of 52%. Unfortunately, a one-pot cross coupling final step could not be accomplished.

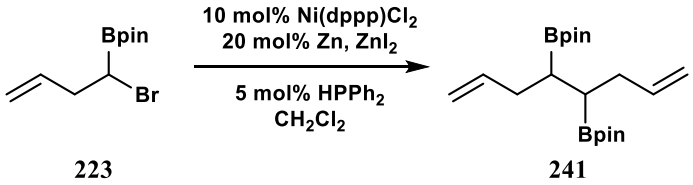
Table 10: Substrate scope for the α- or β-substituted boronic esters.

entry	main diastereomer[a]	*T, t*	yield	*syn*/*anti*
1	 240a	–20 °C, 2 h	97%	95:5
2	 240b	rt, 18 h	71%	76:24

entry	main diastereomer[a]	*T, t*	yield	*syn/anti*
3	 240c	rt, 18 h	71%	<1:99
4	 240d	rt, 18 h	41%	<1:99

a: General conditions: $Ni(dppp)Cl_2$ (10 mol%), Zn, ZnI_2 (20 mol% each), $HPPh_2$ (5 mol%), 1.0 eq homoallyl boronic ester **238**, 1.0 eq aldehyde in dichloromethane (1.0 M). different reaction temperatures and times are listed above. The reaction temperature was adjusted with an acetone or isopropanol/dry ice bath.

When an α-bromo substituted boronic ester (**223** in Scheme 108) was used, the intended isomerization did not proceed. Interestingly, a homocoupling, similar to a Kumada coupling, took place, instead. Diester **241** was exclusively obtained, which could be verified by GC/MS analysis and NMR spectroscopy. This phenomenon was also observed, when simple homoallyl bromide or homoallyl acetates were used for the isomerization process.



Scheme 108: Undesired homocoupling of α-bromo substituted homoallyl boronic ester **223**.

In conclusion, bromo-substituted homoallyl boronic esters as well as alkenyl bromide **242** and acetate, such as **225** (Figure 21), were not suited for an isomerization step as they underwent a nickel-catalyzed homocoupling instead.

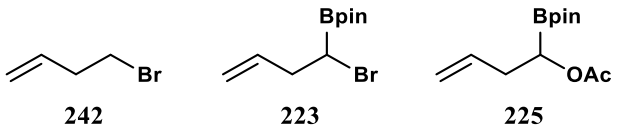


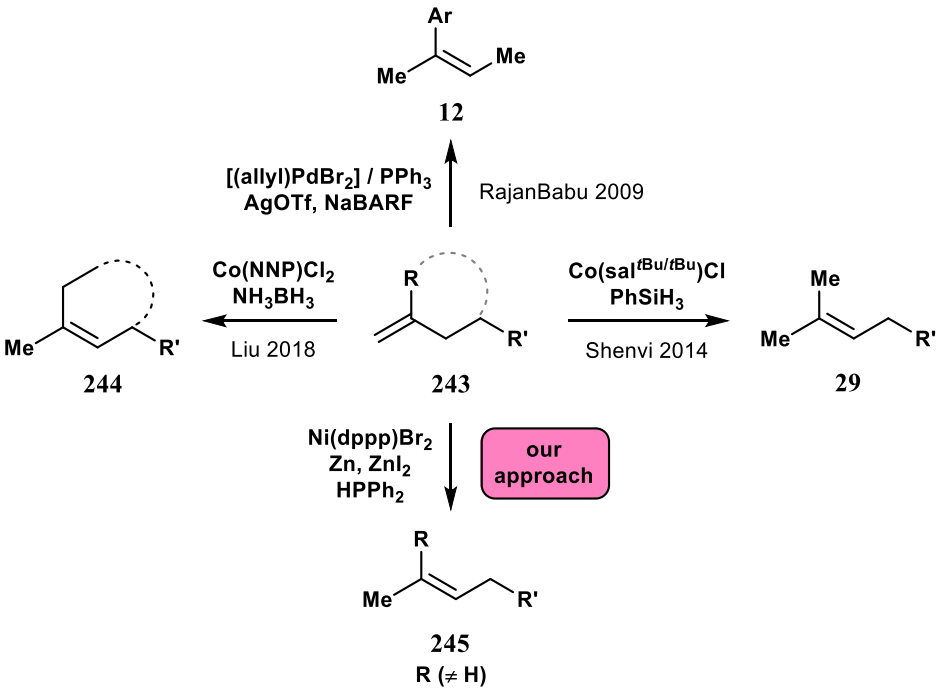
Figure 21: Substrates, not suitable for the nickel-catalyzed isomerization. A homocoupling took place instead.

3.2.5 Isomerization/Allylboration of 1,1-Substituted Homoallylic Boronic Esters

In the last set of experiments, the question should be addressed, whether the double bond transposition could also be performed with homoallyl boronic acid pinacol esters with higher steric demand, such as 1,1-disubstituted substrates with an *exo*-double bond. Before turning attention to boron-containing starting materials, simple aliphatic alkenes were tested, first.

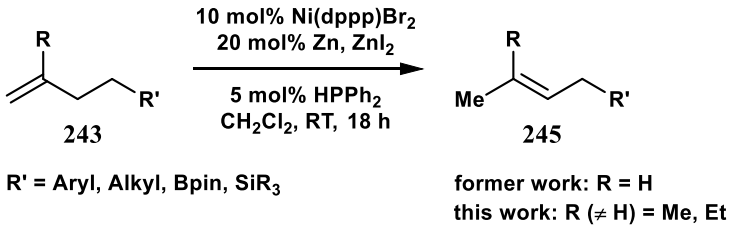
3.2.5.1 Isomerization of 1,1-Substituted Alkenes

As illustrated in the before-mentioned chapter, the nickel-catalyzed double bond transposition is applicable to higher functionalized target molecules as *N*-allyl amides and carbamates. Now, that several functional groups have been successfully addressed, the final question is whether the reaction is also possible for substrates with higher steric demand, such as for those with a 1,1-disubstituted double bond as Shenvi, Liu or RajanBabu already described for their cobalt- and palladium-based catalysts (cf. Scheme 109).[22,29,30]



Scheme 109: Overview of the isomerization of substrates with an *exo*-double bond.

For this purpose, the established nickel catalyst system was first utilized for the isomerization of aliphatic substrates with an *exo*-double bond. The reaction is illustrated in Scheme 110.

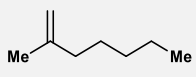
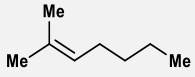
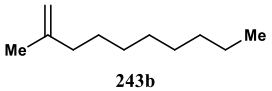
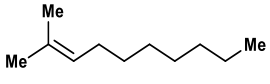
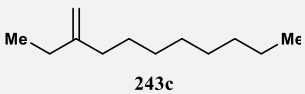
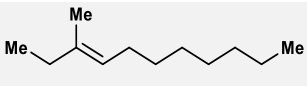


Scheme 110: Desired nickel-catalyzed double bond transposition in 1,1-disubstituted alkenes.

For the isomerization with R = Me, the number of internal isomers of the outcoming trisubstituted alkene was determined *via* GC/MS analysis. The reactions were not purified. Other isomers were formed in inferior amounts, even at ambient temperature, because the trisubstituted double bond is the thermodynamically favored one.

As listed in Table 11, the nickel-catalyst was reactive enough to isomerize sterically more hindered *exo*-double bonds. The above shown isomerization approaches were applied as test reactions for the desired one-pot sequence, combining the isomerization of homoallylic boronic ester with a subsequent allylboration reaction. These experiments should pave the way for further isomerization of boron functionalized 1,1-disubstituted olefins in this reaction sequence.

Table 11: Test reactions for the isomerization of 1,1-disubstituted olefins.

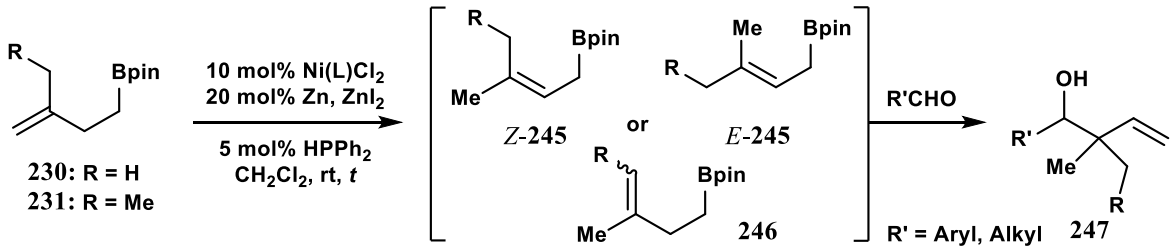
entry	starting material	main isomer[a]	2-alkene[b]	sum of other isomers[b]
1	 243a	 245a	65%	35%
2	 243b	 245b	66%	34%
3	 243c	 245c	54% *E* only	46%

a: General conditions: $Ni(dppp)Br_2$ (10 mol%), Zn, ZnI_2 (20 mol% each), $HPPh_2$ (5 mol%), 1.0 eq olefin in dichloromethane (1.0 M). Stirring at rt for 18 h; b: Isomeric mixture of the product was analyzed *via* GC/MS only.

3.2.5.2 Isomerization/Allylboration of 1,1-Substituted Homoallylic Boronic Esters

Initially, the possibility of realizing an isomerization of an *exo*-chain double bond of a 1,1-disubstituted homoallyl boronic ester was investigated. The isomerization should occur towards the boron functionality and thereby generate a geminal-dimethyl (**230**, R = H) subunit. If the substituent R in Scheme 111 is no hydrogen, but a methyl group (compound **231**), an interesting scenario would occur. The double bond can either isomerized toward the functional group to

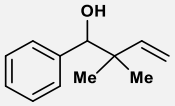
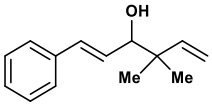
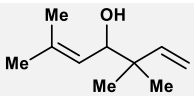
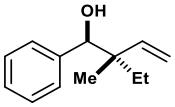
ensure the generation of the proposed intermediate *Z*/*E*-**245** which would react with the desired aldehyde to generate the allylboration product **247**. Intermediate **246** would probably resemble a dead-end and lead to a loss in efficiency. Both intermediates possess a trisubstituted double bond that likely does not exhibit a significant reactivity for the nickel catalyst or a driving force toward one or the other transposition to convert *Z*/*E*-**245** into **246**, or vice versa.[125]

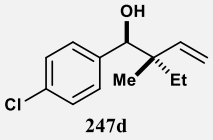
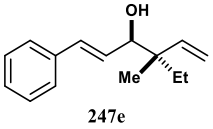
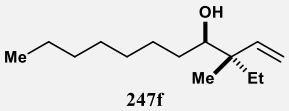
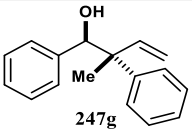


Scheme 111: Isomerization/allylboration of homoallylic boronic esters with an *exo*-double bond.

By using 1,1-disubstituted starting materials, the sequence would allow the formation of a quaternary chiral carbon center in the proposed product **247**. Due to the fact, that *exo*-double bonds are more difficult to isomerize, the reaction was carried out at ambient temperature instead of temperatures below 0 °C. A screening with different ligands and reaction temperatures was necessary to find the right conditions forcing the double bond to isomerize to the desired allylic position. In terms of reactivity and selectivity Ni(dppm)Br_2 acted superior to the usually used Ni(dppe)Cl_2 or Ni(dppp)Br_2 pre-catalysts, which themselves resulted in unsatisfying conversion of the starting material (**231**, R = Me). Table 12 summarizes the results.

Table 12: Isomerization/allylboration of homoallylic substrates with *exo*-double bond.

entry	main product[a]	M(L)X_2	*T*, *t*	yield	*syn*/*anti*
1	 247a	Ni(dppp)Br_2	rt, 16 h	75%	-
2	 247b	Ni(dppp)Cl_2	rt, 16 h	81%	-
3	 247c	Ni(dppp)Br_2	rt, 16 h	80%	-
4	 130	Ni(dppm)Br_2	rt, 48 h[b]	43%	19:81

entry	main product[a]	M(L)X_2	*T*, *t*	yield	*syn*/*anti*
5	 **247d**	Ni(dppm)Br_2	rt, 48 h[b]	73%	33:67
6	 **247e**	Ni(dppm)Br_2	rt, 48 h[b]	67%[c]	23:77
7	 **247f**	Ni(dppm)Br_2	rt, 16 h[b]	52%	31:69
8	 **247g**	Ni(dppp)Cl_2	80 °C, 18 h	63%	<1:99

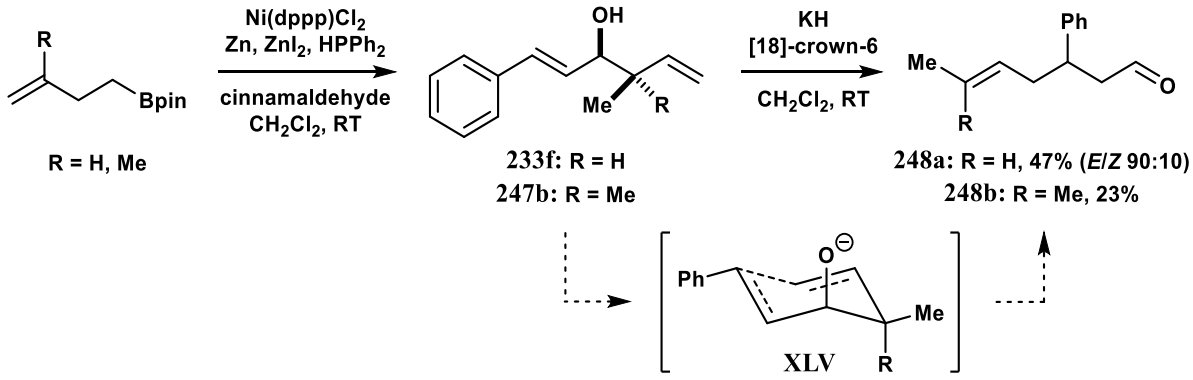
a: General conditions: Ni(L)X_2 (10 mol%), Zn, ZnI_2 (20 mol% each), $HPPh_2$ (5 mol%), 1.0 eq homoallyl boronic ester **230** or **231** and aldehyde. Stirring at rt. Different reaction times are listed above; b: The isomerization was performed first in absence of the aldehyde. The aldehyde was added after stirring at rt o/n; c: The product mixture contained 11 mg (20%) of unreacted cinnamaldehyde which could not be removed by multiple column chromatography.

The *exo*-chain double bond derivative **230** (R = H) reacted very slowly. However, at room temperature after longer reaction times and catalyst addition, the desired homoallylic alcohols with a quarternary carbon-atom (**247a+b**) were obtained in acceptable yields of 75% and 81% (Table 12, entries 1 and 2). Noteworthy, the natural product *artemisia alcohol* **247c** could be isolated as racemate in 80% yield in one single step (entry 3). Moreover, the transpositions of starting material **231** (R = Me) gave the *anti*-configured products predominantly. This means, with respect to the methyl group, the isomerization proceeded in a *Z*-selective fashion. The rationale for the formation of the *anti*-configured products was that the transposition proceeded predominantly through intermediate *E*-**245**. The diastereomeric ratios were only moderate up to 81:19 *anti*/*syn* ratio and 73% yield. The reason can be found in the undesired, but possible formation of by-product **246** (Scheme 111), in which a trisubstituted double bond was also formed, located in the homoallylic position, though, not undergoing the desired allyboration.[125]

3.2.5.3 One-Pot Isomerization/Allylboration/Oxy-Cope Rearrangement Sequence

Homoallylic alcohols **233f** and **247b**, derived from cinnamaldehyde, were qualified for a third reaction in a row, since they contained a 1,5-dien-3-ol structure motif for a possible anionic Oxy-Cope rearrangement. Through this process, δ,ε-unsaturated aldehydes could be generated.

The rearrangement was realized by adding potassium hydride and [18]-crown-6 to the raw isomerization/allylboration mixtures. Scheme 112 shows the threefold reaction sequence.[129]

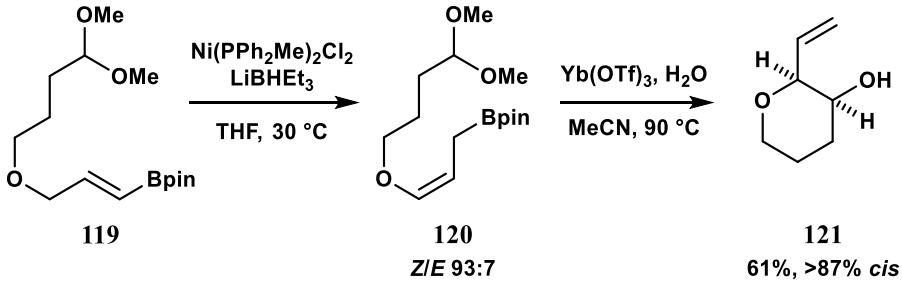


Scheme 112: Isomerization/allylboration/Oxy-Cope rearrangement sequence.

The anionic Oxy-Cope rearrangement proceeded very fast. The reaction passed again a six-membered Zimmerman-Traxler transition state (**XLV**). Both aldehydes **248a** and **248b** could be obtained in moderate yields of 47% and 23%, respectively, in this three-step sequence. In product **248a** the *E*-isomer predominated (*E*/*Z* = 90:10), since the formation of the enolate form was energetically favored. The sterically demanding groups (Me, Ph) were located in the equatorial position.

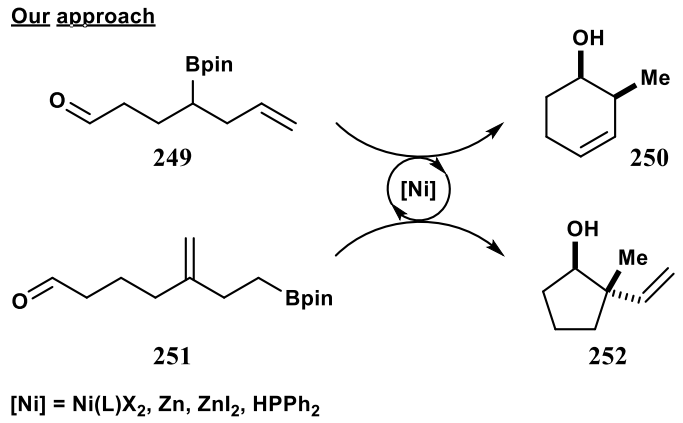
3.2.6 Intramolecular Isomerization/Allylboration Sequence

The applicability of the reaction sequence shall finally be verified for an intramolecular variant. Inspired by the work of Miyaura,[74] who realized an intramolecular isomerization/allylboration process *via* isomerization away from the boron functionality towards the formation of the thermodynamically stable enolether **120** as driving force of the isomerization (Scheme 113). This enables a convenient practicability of this type of substrates.[74]



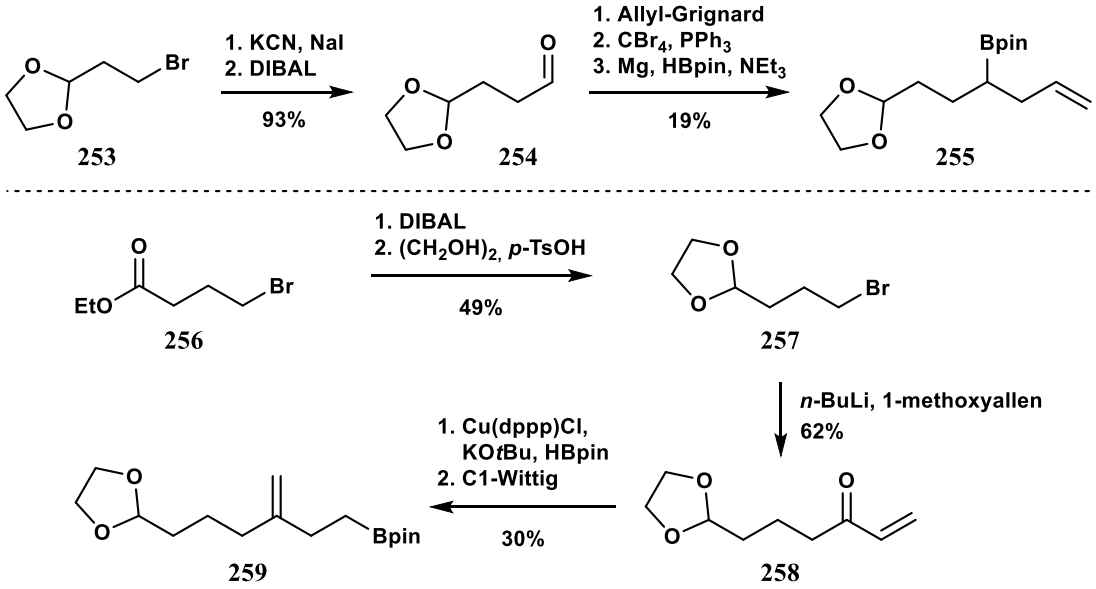
Scheme 113: Intramolecular Isomerization/Allylboration Sequence by Miyaura.

Aldehydes **249** and **251** in Scheme 114 were selected as potential substrates to realize such a process towards a diastereoselective formation of unsaturated cyclic alcohols **250** and **252**. The double bond transposition shall, again, proceed towards the boronic ester moiety.



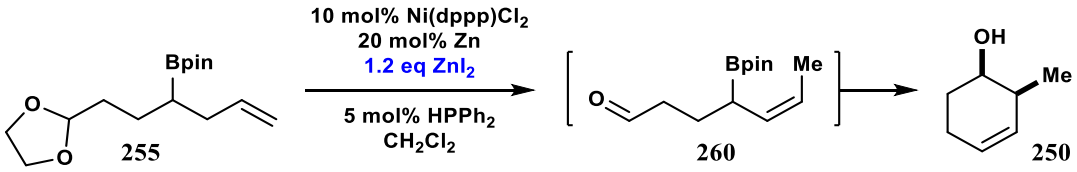
Scheme 114: Idea for the intramolecular isomerization/allylboration sequence.

The acetal protected starting materials **255** and **259** were synthesized in simple five-step sequences in moderate overall yields starting from commercially available starting materials. They are shown in Scheme 115. Bromide **253** was converted into the corresponding nitrile, first, before being reduced with di*iso*butyl aluminum hydride (DIBAL) to aldehyde **254**. The subsequent Grignard and Appel reactions are followed by a final Grignard-type reaction introducing pinacol boronic ester **255** in an acceptable overall yield of 18% over five linear steps. Homoallyl boronic ester **259**, containing an *exo*-double bond, was synthesized by DIBAL-reduction of commercially available ethyl 4-bromobutanoate (**256**), followed by acetal-protection and enone-formation with methoxyallen to α,β-unsaturated ketone **258** in 30% yield over three steps. The final copper-catalyzed hydroboration and Wittig reactions give target molecule **259** in 9% overall yield.



Scheme 115: Syntheses of acetal-protected homoallyl boronic esters **255** and **259**.

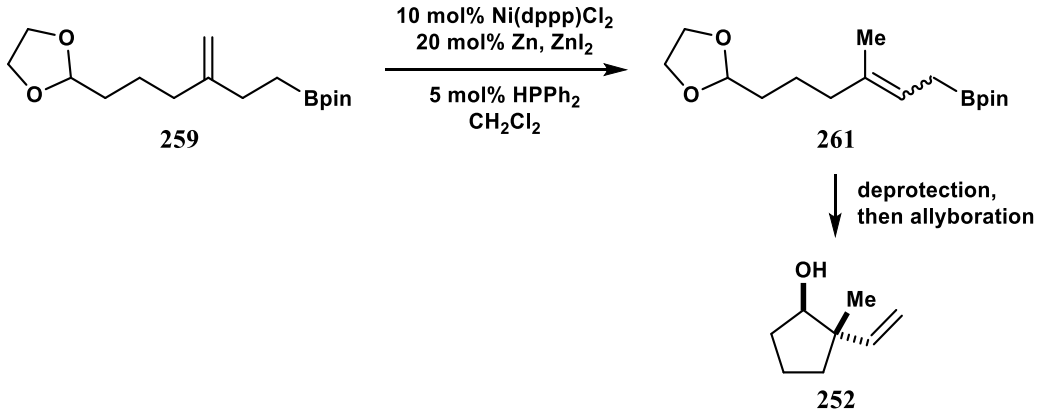
As usual, the intramolecular isomerization/allylboration process should be realized by reacting the starting materials with the nickel catalyst system. The first idea was to use stoichiometric amounts of the Lewis acid zinc iodide to activate the nickel catalyst on the one hand and deprotect the acetal on the other, enabling a direct intramolecular cyclization *via* allylboration to occur. The reaction is illustrated in Scheme 116 with boronic ester **255** in an exemplary way.



Scheme 116: Proposed nickel-catalyzed isomerization/*in situ* intramolecular allylboration *via* ZnI_2-mediated acetal-deprotection.

For acetal deprotection, 1.2 eq ZnI_2 were used instead of 20 mol%. Unfortunately, a deprotection was not detected *via* GC/MS-analysis, just an unselective isomerization of **255** with a *Z*/*E*-ratio of 67:33. Since the deprotection did not take place, the intramolecular allylboration was pending. The same phenomenon was observed when the 1,1-disustituted homoallyl boronic ester **259** was used. Either way, the isomerization had to be done at ambient temperature. At lower temperatures, the reaction did not proceed at all.

Since it was possible to at least isomerize the starting material, (Lewis or Brönstedt) acidic conditions, potentially enabling a subsequent intramolecular allylboration, were further investigated. The isomerization was performed first. The acid was added afterwards to the reaction mixture in order not to bother the preceding isomerization step.



Scheme 117: Isomerization, first. Then desired deprotection and cyclization.

Table 13 summarizes the reactions.

Table 13: Approaches concerning the acetal deprotection after isomerization.

entry	reagents	solvent	*T*, *t*	reaction progress
1	10 mol% $InCl_3$	MeOH/H_2O (1:1)	90 °C, 18 h	decomposition
2	2.5 eq CAN	MeCN/H_2O (1:1)	65 °C, 18 h	decomposition
3	10 mol% I_2	acetone	rt, 18 h	decomposition
4	50 mol% AcOH	MeOH/H_2O (1:1)	rt, 18 h	no conversion
5	1.0 eq *p*-TsOH	MeOH/H_2O (1:1)	rt, 18 h	decomposition
6	10 mol% $FeCl_3$	-	rt, 24 h	partial conversion
7	SiO_2	acetone	rt, 5 d	no conversion
8	$BF_3 \cdot OEt_2$	CH_2Cl_2	rt, 18 h	decomposition
9	**20 mol% $TiCl_4$**	**CH_2Cl_2**	**rt, 18 h**	**product detectable in GC/MS; no isolation possible**
10	$Yb(OTf)_3$	MeCN or THF	rt, 18 h	decomposition

Nearly all attempts to deprotect the acetal, except for entries 6 and 9 in Table 13, failed. They led to decomposition of the starting material **261**. With catalytic amounts of $FeCl_3$ or $TiCl_4$, the aldehyde form of alkene **261** could be detected *via* GC/MS analysis, but a subsequent allylboration did not take place.

An isomerization of acetal-protected homoallyl boronic esters **255** and **259** was successful, albeit with lower isomeric excess of *Z*/*E* ~2:1. Unfortunately, an *in situ* cyclization by intramolecular allylboration could not be realized due to deprotection issues of the acetal group. A dimethyl acetal would be probably better suited, since the stability against acidic conditions is lower than with the ethylene glycol acetal.

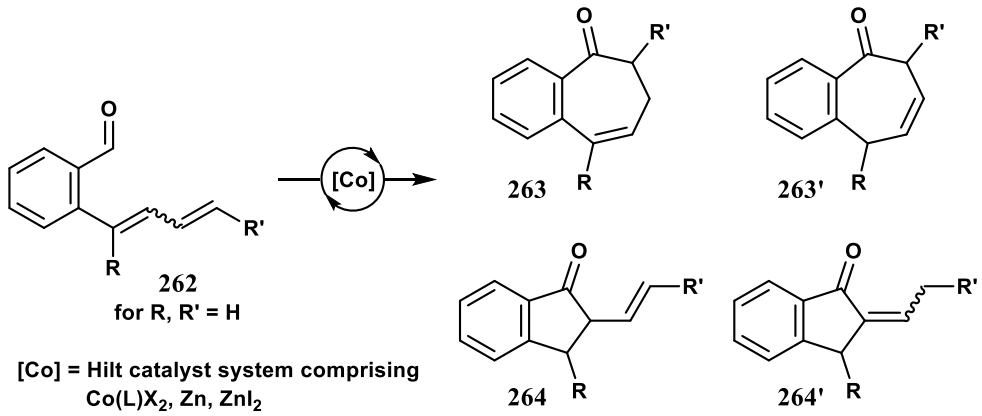
In conclusion, the established nickel-catalyzed isomerization of terminal alkenes is possible in the presence of an aldehyde. The carbonyl moiety did not interfere with the catalyst system, enabling a subsequent highly diastereoselective allylboration when homoallylic boronic esters were transferred to their *Z*-configured crotyl species. Nevertheless, this multistep sequence was limited to an intermolecular variant.

The method is leaving the question, if the versatile carbonyl moiety could also be applied in other nickel- or cobalt-catalyzed transformations, which were not yet addressable by the Hilt group. A hydroacylation would be an attractive target reaction.

3.3 Cobalt-Catalyzed Reductive Cyclization of 1,3-Dienes

In 2014, the Dong group presented an intermolecular hydroacylation of 1,3-dienes in the presence of a cobalt catalyst and appropriate reductants to form the active cobalt(I) species.[97] Further, they described an intramolecular hydroacylation of alkenes for the formation of four-membered target structures (see Schemes 53 and 56).[99] Since their reaction conditions were quite similar to the Hilt group's, the question arose, if a hydroacylation of 1,3-dienes would also be possible with Hilt's established cobalt catalyst system ($Co(L)X_2$, Zn, ZnI_2) which was already successfully applied for other formal cycloaddition reactions (for selected examples, see chapter 1.3.1).

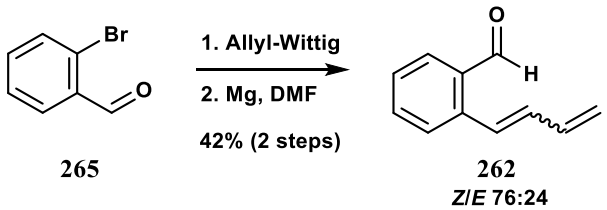
In order to reduce the number of possible regioisomers, an intramolecular variant of the hydroacylation was targeted, using 2-(buta-1,3-dien-1-yl)benzaldehyde (**262**) as test substrate. Diene **262** can either undergo the desired cyclization with the terminal double bond providing a seven-membered ring **263** or with the internal double bond leading to product structures of type **264**.



Scheme 118: Proposed conjugate intramolecular hydroacylation of 1,3-diene **262** with possible regioisomers.

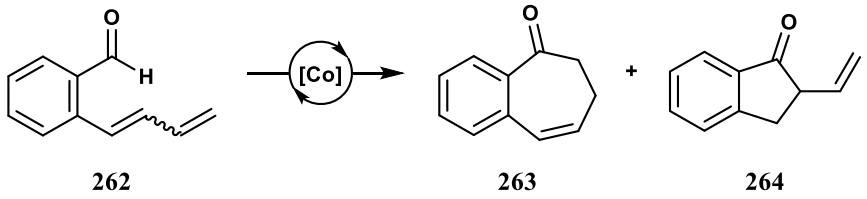
3.3.1 Optimization of Reaction Parameters

1,3-Diene **262** (with R, R' = H) could be easily prepared in a two-step synthesis comprising a Wittig olefination of 2-bromo benzaldehyde (**265**) followed by a subsequent Grignard reaction in 42% overall yield and a *Z*/*E*-ratio of 76:24.



Scheme 119: Synthesis of (*Z*/*E*)-2-(buta-1,3-dien-1-yl)benzaldehyde.

Diene **262** was then reacted with the cobalt catalyst according to a general procedure (in the following referred to as GP 9) using Co(L)Br_2, Zn, and ZnI_2 under different reaction conditions to initiate the desired transformation and to find out which regioisomers could be addressed. The reaction conditions are summarized in Table 14.



262 **263** **264**

Scheme 120: Potential cobalt-catalyzed intramolecular hydroacylation.

Table 14: Screening of reaction conditions for the cobalt-catalyzed intramolecular cyclization of 1,3-diene **262**.

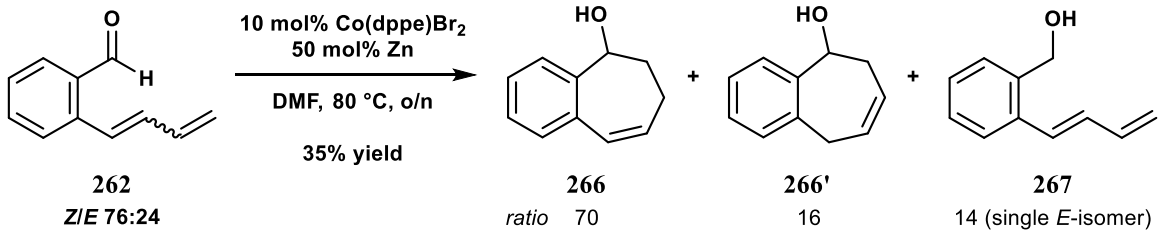
entry	[Co][a]	solvent	*T*, *t*	reaction progress[b]
1	10 mol% Co(dppe)Br_2 20 mol% Zn, ZnI_2	CH_2Cl_2	rt, o/n	no conversion
2	10 mol% Co(dppe)Br_2 50 mol% Zn	CH_2Cl_2	rt, o/n	no conversion
3	10 mol% Co(dppe)Br_2 50 mol% Zn	MeCN	rt, o/n	no conversion
4	10 mol% Co(dppe)Br_2 50 mol% Zn	MeCN	80 °C, o/n	no conversion, partial reduction of s.m.
5	10 mol% Co(dppe)Br_2 50 mol% Zn	toluene	rt, o/n	no conversion
6	10 mol% Co(dppe)Br_2 50 mol% Zn	toluene	80 °C, o/n	no conversion, partial reduction of s.m.
7	10 mol% Co(dppe)Br_2 50 mol% Zn	DMF	rt, o/n	44% conversion, **3 new peaks in GC/MS**
8	10 mol% Co(dppe)Br_2 50 mol% Zn	DMF	80 °C, o/n	**full conversion,** **3 new peaks in GC/MS**
9	10 mol% Co(dppe)Br_2 50 mol% Zn	DMF	80 °C, o/n	35%[c] (3 products in NMR)
10	10 mol% Co(dppe)Br_2 150 mol% Zn	DMF	80 °C, o/n	32%[c] (3 products in NMR)

entry	[Co][a]	solvent	*T*, *t*	reaction progress[b]
11	**10 mol% Co(dppe)Br$_2$ 150 mol% Zn**	**DMF**	**rt, o/n**	**48%**[c] (3 products in NMR)
12	10 mol% Co(dppe)Br$_2$ 150 mol% Zn, 40 mol% ZnI$_2$	DMF	rt, o/n	impurities in GC/MS
13	no cobalt catalyst, 150 mol% Zn	DMF	rt or 80 °C, o/n	no reaction[d]
14	10 mol% Co(dppe)Br$_2$ no Zn	DMF	rt or 80 °C, o/n	no conversion
15	20 mol% ZnI$_2$, 50 mol% Zn	DMF	80 °C, o/n	decomposition
16	aldehyde **262** only	DMF	80 °C	partial decomposition

a: General conditions: Co(L)X$_2$ (10 mol%), Zn (20 - 150 mol%), solvent. First, the cobalt catalyst and Zn were suspended in the solvent and stirred for 10 min at rt until substrate **262** (0.5 M) was added and the reaction was stirred overnight at the desired temperature; b: Monitoring of the reaction was performed without internal standard to reveal conversion of the s.m.; c: Isolated yield after purification by FC (*n*-pentane/Et$_2$O 4:1); d: Partial reduction of the aldehyde was detected *via* GC/MS analysis.

As can be seen in Table 14 (entry 1), the initial cobalt catalyst system in dichloromethane did not provide any product. The reaction in dichloromethane also failed when using different amounts of the catalyst components (entry 2). When changing the solvent to MeCN or toluene (entries 3-6) the reaction did not proceed, either. In toluene, the catalyst was barely soluble. When *N*,*N*-dimethyl formamide (DMF) was applied as solvent and 50 mol% Zn were used (entry 7), the corresponding gas chromatogram (GC/MS analysis) showed three new peaks with a mass-to-charge ratio (m/z) of 160 u indicating that a reduction process, similar to a Prins reaction, instead of a hydroacylation took place. When raising the temperature to 80 °C and the amount of Zn powder to 150 mol% (entry 9), the amount of the new products could be increased with full conversion of the starting material **262**. NMR characterization of the product underlined the result that no hydroacylation, but a reductive cyclization occurred. The hydroxyl group of the product mixture (**266**, **266'**, and **267** in Scheme 121) could further be detected *via* infrared (IR) spectroscopy. A carbonyl band was no longer visible.

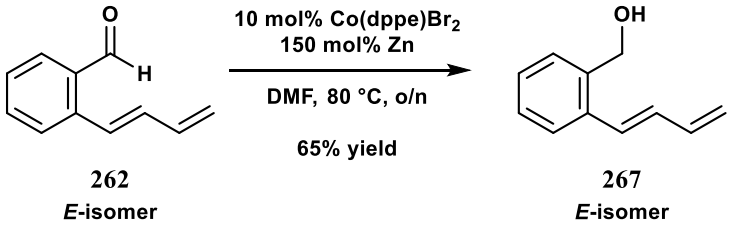
The terminal double bond of 1,3-diene **262** potentially acts as nucleophile letting the other double bond remain in place. As by-product, the seven-membered ring with the isomerized double bond (**266'**) could be detected and characterized by NMR spectroscopy.



Scheme 121: Product spectrum of the cobalt-catalyzed conjugate reductive cyclization.

The second by-product was the reduced starting material with an *E*-configured double bond, leading to the assumption that only the *Z*-configured isomer of the starting material **262** underwent the cyclization, whereas the *E*-configured part of the starting material was solely reduced by Zn.

To underline this hypothesis, *E*-configured 2-(buta-1,3-dien-1-yl)benzaldehyde was synthesized in a three-step sequence and then reacted with the initial cyclization conditions, shown in Scheme 122. Benzyl alcohol **267** was a result of the reduction of *E*-configured starting material and was isolated in 65% yield. At 80 °C reaction temperature, a polymerization of the starting material cannot be excluded.



Scheme 122: Reduction of the *E*-configured 1,3-diene to benzylic alcohol **267**.

To exclude a background reaction, the cyclization was also performed without Co(dppe)Br_2 (entries 13+15 in Table 14), without Zn powder (entry 14) and completely without any reagent (entry 16). In all cases, no reaction occurred. At 80 °C, it was assumed that partial polymerization of the starting material could occur. Therefore, the reaction temperature was reduced to ambient temperature, thus the isolated yield of the product mixture could be increased from initial 35% to 48%.

In the literature, other reductants than Zn powder were used for hydroacylation reactions.[100,101] Consequently, other reductants were screened for the newly developed intramolecular cyclization (Table 15).

Table 15: Reductant screening.

entry	[Co][a]	solvent	*T*, *t*	reaction progress
1	10 mol% Co(dppe)Br_2 150 mol% Zn	DMF	rt, o/n	**48%**
2	10 mol% Co(dppe)Br_2 150 mol% In	DMF	rt, o/n	no reaction
3	10 mol% Co(dppe)Br_2 150 mol% Mn	DMF	rt, o/n	no reaction
4	10 mol% Co(dppe)Br_2 150 mol% Mg[b]	DMF	rt, o/n → 80 °C, o/n	no reaction, then decomposition

a: General conditions: Co(L)X_2 (10 mol%), Zn (20 - 150 mol%), solvent. First, the cobalt catalyst and Zn were suspended in the solvent and stirred for 10 min at rt until substrate **262** (0.5 M) was added and the reaction was stirred overnight at the desired temperature; b: Another portion of catalyst and reductant was added and the reaction was stirred overnight at 80 °C.

No reaction occurred when Mn or In powder was used instead of Zn (entries 2 and 3). Only Mg (150 mol%, entry 4) showed enhanced reactivity at 80 °C. Unfortunately, the reaction with Mg lead to decomposition of the starting material and the formation of undefined product species (detectable *via* GC/MS analysis).

Finally, different ligands were tested, anticipating that dppe already was the ligand of choice. Bidentate ligand dppp acted similar to dppe (entry 2), whereas all other substituted dppp derivatives resulted in no conversion at all (entries 3-6). The reaction temperature of 80 °C was applied to ensure full conversion of the starting material. Imine-based ligand py-imin (entry 7) gave a change in regioselectivity, since the double bond isomerizes within the ring to a new **266**:**266'** ratio of 44:56. Nitrogen-containing ligands could be a good alternative to phosphine ligands to address isomer **266'** more regioselectively.

Table 16: Ligand screening.

entry	[Co][a]	solvent	*T*, *t*	reaction progress[b]
1	10 mol% Co(dppe)Br_2 150 mol% Zn	DMF	80 °C, o/n	**266**:**266'** = 81:19
2	10 mol% Co(dppp)Br_2 150 mol% Zn	DMF	80 °C, o/n	**266**:**266'** = 78:22
3	10 mol% Co(dpppMe$_2$)Br_2 150 mol% Zn	DMF	80 °C, o/n	no conversion

entry	[Co][a]	solvent	*T*, *t*	reaction progress[b]
4	10 mol% $Co(bdpp)Br_2$ 150 mol% Zn	DMF	80 °C, o/n	no conversion
5	10 mol% $Co(dpppBuEt)Br_2$ 150 mol% Zn	DMF	80 °C, o/n	no conversion
6	10 mol% $Co(PPh_3)_2Br_2$ 150 mol% Zn	DMF	80 °C, o/n	no conversion
7	10 mol% Co(py-imin[c])Br_2 150 mol% Zn	DMF	80 °C, o/n	**266**:**266'** = 44:56

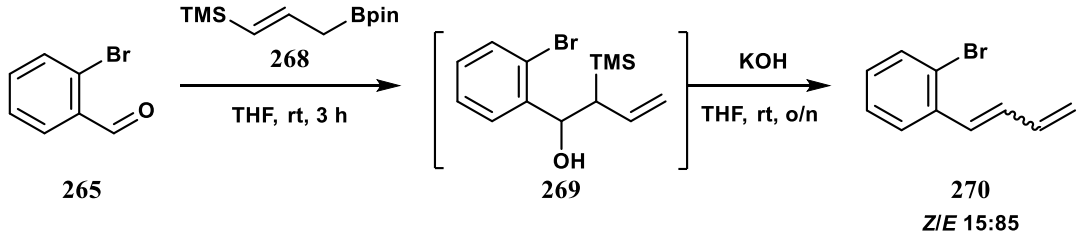
a: General conditions: $Co(L)X_2$ (10 mol%), Zn (150 mol%) in DMF. First, the cobalt catalyst and Zn were suspended in the solvent and stirred for 10 min at rt, until aldehyde **262** (0.5 M) was added and the reaction was stirred overnight at the desired temperature; b: The reaction progress and the isomeric ration were monitored by GC/MS analysis; c: py-imin = (*E*)-2-((pyridin-2-ylmethylene)-amino)ethan-1-amine.

After this examination, it was clear that under reductive conditions, the cyclization was only successful with the *Z*-configured starting material *Z*-**262**. A stoichiometric amount of Zn powder (150 mol%) is necessary for the formation of the active Co(I) species on the one hand and the reduction of the product on the other.

3.3.2 Reductive Cyclization with the Z-Configured Diene

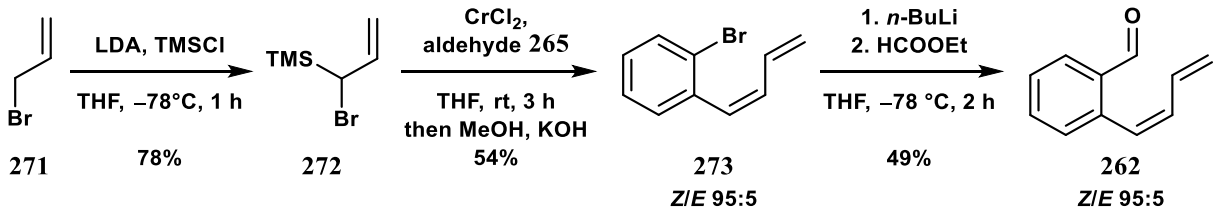
After initial studies and optimization of the parameters towards a reductive cyclization, the optimization of the yield of the dihydrobenzoannulenol target structures **263** was addressed. The synthesis of pure *Z*-configured 1,3-diene was necessary to prevent the corresponding *E*-configured isomer from solely being reduced to benzyl alcohol **267**. In the literature, there are some approaches towards the synthesis of *Z*-configured double bonds in styrene position.[130,131]

First, it was planned to address the product by a Peterson-like olefination/elimination sequence according to a procedure of Stupp.[131] Unfortunately, an isomeric mixture of 1,3-diene **270** with a high *E*-isomeric excess (*E*/*Z* = 85:15, monitored *via* GC/MS, Scheme 123) was obtained.



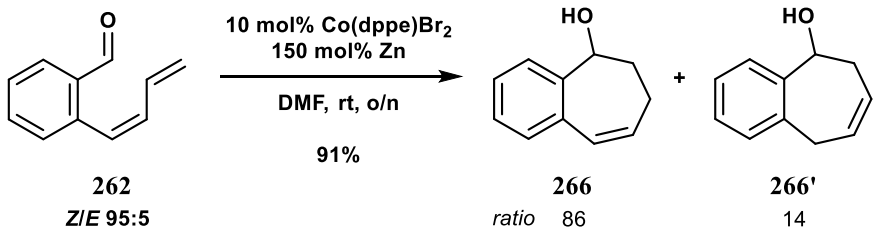
Scheme 123: Allylboration/elimination sequence according to a procedure of Stupp.[131]

Changing the conditions to a *Z*-selective Takai-type olefination with $CrCl_2$ and basic work-up (6 M KOH), the *Z*-configured bromide **273** could be obtained in acceptable yield of 54% and good *Z*/*E* ratio. Subsequent debromocarbonylation at low temperatures provided the desired *Z*-configured aldehyde **262** in moderate yield (49%) with a *Z*/*E* ratio of 95:5 (Scheme 124).



Scheme 124: Three-step synthesis of *Z*-configured 1,3-diene **262**.

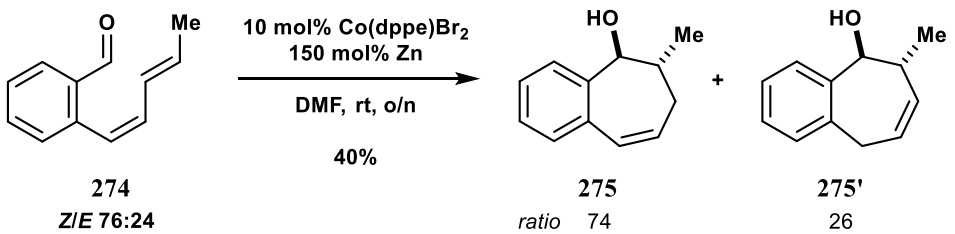
Since the yield was not satisfactory when the isomeric mixture of 1,3-diene **262** was used, the cyclization in DMF with 10 mol% $Co(dppe)Br_2$ and 150 mol% Zn powder was performed again with the pure *Z*-configured isomer in hand.



Scheme 125: Cobalt-catalyzed reductive cyclization of (*Z*)-2-(buta-1,3-dien-1-yl)benzaldehyde.

As expected, the reaction proceeded smoothly at ambient temperature leading to a dramatic increase in yield (91%) and improved regioisomeric ratio (*r.r.*) **266**:**266'** of 86:14. The uncyclized by-product **267** was not observed any longer. But even with isomerically enriched 1,3-diene, the formation of isomer **266'** could not be completely suppressed. The formation of **266'** could be a result of the ring isomerization of preformed isomer **266** during the Prins-like cyclization running through a carbocation species. Katja Feismann is thankfully acknowledged for the optimization of reaction parameters.[132]

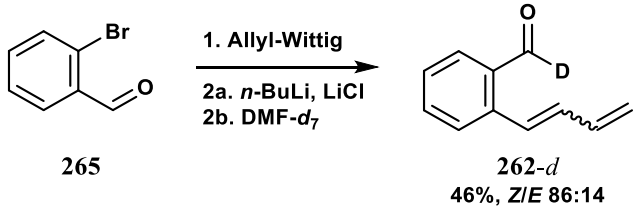
Cyclization of the methyl-substituted 1,3-diene derivative **274** gave **275** in moderate yield as Scheme 126 depicts. The substrate scope of the reaction is under ongoing investigation in our group.



Scheme 126: Intramolecular conjugate cyclization of 2-((1*Z*,3*E*)-penta-1,3-dien-1-yl)benzaldehyde (**274**).

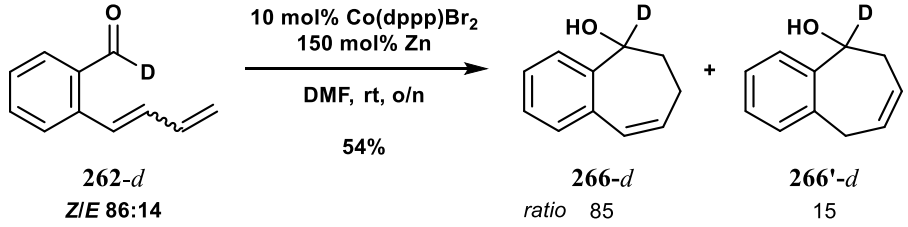
3.3.3 Initial Mechanistic Investigations

For the reduction process, the electrons are presumably provided by stoichiometric amounts of Zn powder. To reveal the origin of the necessary protons, initial mechanistic investigations were performed using the formyl-deuterated starting material **262**-*d*, which was synthesized in a two-step synthesis with 46% overall yield (Scheme 127).



Scheme 127: Synthesis of deuterated 2-(buta-1,3-dien-1-yl)benzaldehyde.

The substrate was cyclized according to GP 9. The deuterium atom remained at its place and **266**-*d* could be obtained in an isomeric mixture of 85:15.



Scheme 128: Cobalt-catalyzed reductive cyclization of **262**-*d*. The deuterium atom remains at the benzylic position.

As distinguished from Dong's proposed mechanism (see Scheme 54),[97] the deuterium atom stays at its position. The cyclization can be seen as formal intramolecular nucleophilic attack of the terminal double bond of the 1,3-diene subunit to the formyl group in the manner of a Prins reaction. The cobalt catalyst could serve as Lewis acid. In conclusion, no Co–D species is formed *via* β-hydride elimination during the process. The electrons are provided by Zn. A possibility as origin for protons is the solvent. When the reaction was performed in anhydrous DMF-d_7, no incorporation of deuterium was detected *via* GC/MS and NMR analysis, though. When 2.0 equivalents (eq) deuterium oxide were added to the reaction mixture, the isotope incorporation could not reliably be detected. Additional mechanistic investigations are currently underway.

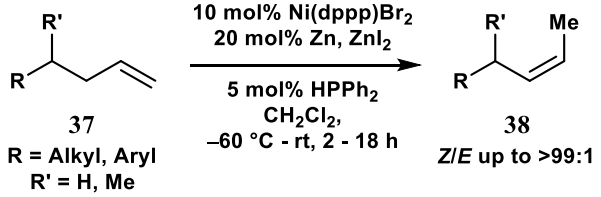
In the course of this work, a reliable basis was provided to broaden the Hilt group's expertise concerning new cobalt-catalyzed transformations of 1,3-dienes and carbonyl compounds. The cobalt-catalyzed intramolecular reductive cyclization of 1,3-dienes is now at a stage where conversion of the starting material as well as yield were already improved. Only the *Z*-

configured 1,3-diene can undergo the transformation. Therefore, the reaction could also be used as an elegant separation of isomeric mixtures of 1,3-dienes, which are often obtained when a Wittig olefination with an allylphosphonium salt is performed. The method is still a research topic in our group and will be further examined by Sebastian M. Weber.

4. Summary and Outlook

4.1 Nickel-catalyzed *Z*-Selective Isomerization of Terminal Alkenes

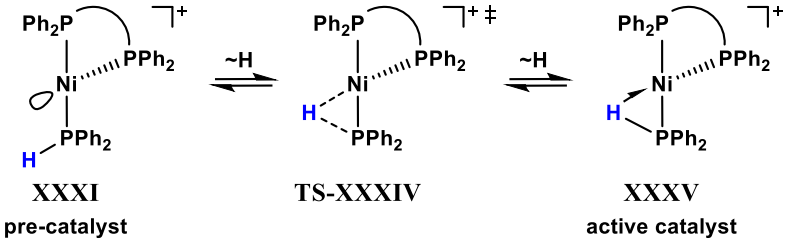
In this dissertation, the mechanism of the nickel-catalyzed *Z*-selective isomerization of terminal alkenes with the additive diphenylphosphine could be successfully clarified.



Scheme 129: Nickel-catalyzed *Z*-selective isomerization of terminal alkenes.

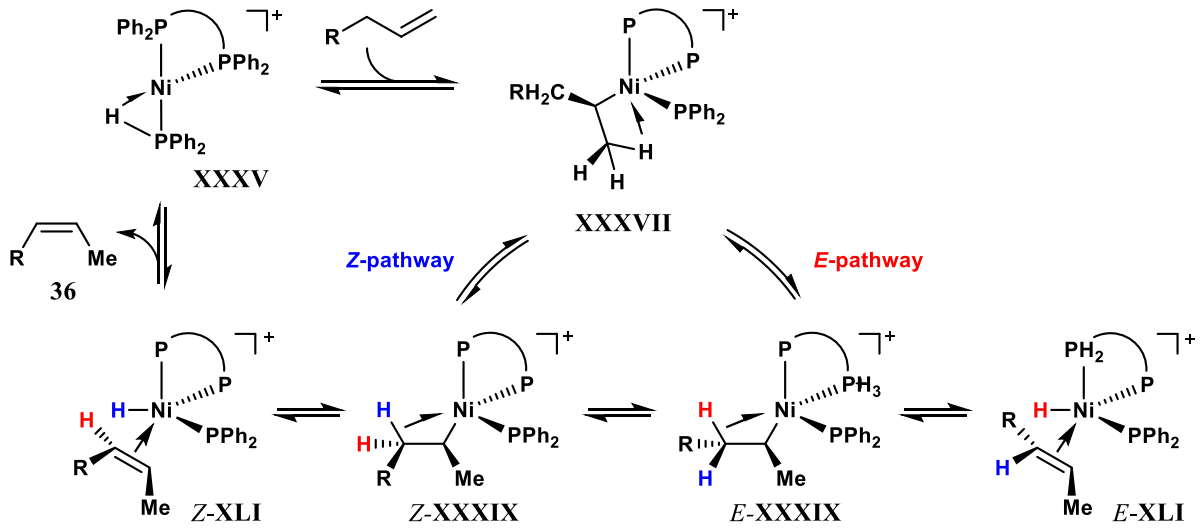
A verification of the postulated nickel(I) as well as cobalt(I) species was achieved by cyclic voltammetry. Further, the existence of a paramagnetic nickel(I) species could be verified *via* qualitative EPR.[103]

In cooperation with Prof. Dr. Robert Berger and Evgeny I. Grigoryev, the mode of action of the additive $HPPh_2$ could be clarified through DFT-calculations. They led to the result that the co-ligand transfers the hydrogen directly to the substrate to initiate the isomerization process. A three-membered transition state **TS-XXXIV** is passed for the activation of the pre-catalyst **XXXI**. The active catalyst species **XXXV** is stabilized by an α-agostic interaction with a Ni–H-bond order of 0.3 and a P–H bond order of 0.6 (Scheme 130). The Ni–H–P arrangement is a 3-center-2-electron bond according to Wiberg bond indices.[110]



Scheme 130: Formation of the active nickel catalyst species **XXXV**.

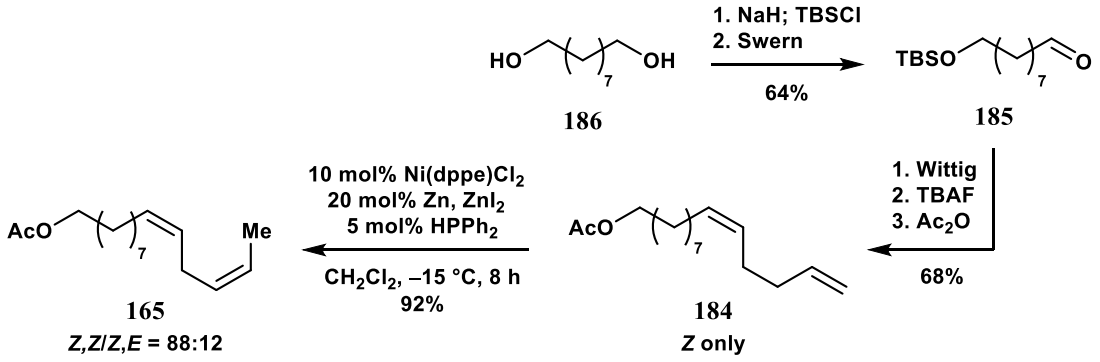
The *Z*-Selectivity of the isomerization process arises at the final step, the β-hydride elimination, which occurs from β-agostic complex **XXXIX**, in which the methyl group and the rest R are predominantly arranged in *syn*-conformation. The active catalyst species **XXXV** is reformed after the release of the 2-alkene **36** (shown for the *Z*-configured alkene in Scheme 131). Calculated and experimental *Z*/*E* ratios of selected isomerization products are in good agreement to each other.[110]



Scheme 131: *β*-Hydride elimination as selectivity-determining step in the calculated alkyl mechanism.

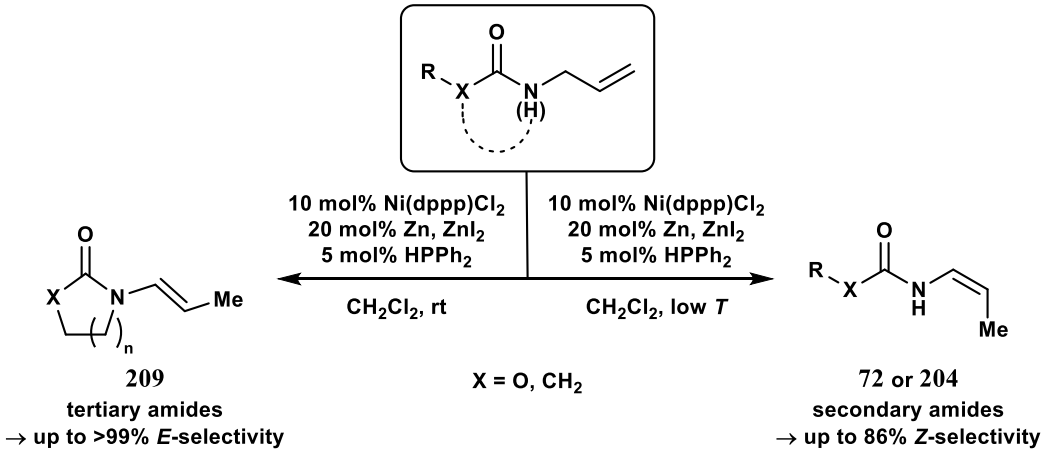
The isomerization of allylbenzene derivatives always proceeded *E*-selectively. In this case, it was assumed that the isomerization runs through a *π*-allyl mechanism, as could be verified by DFT calculations and deuteration experiments.

The nickel-catalyzed *Z*-selective isomerization of terminal alkenes was successfully applied as key step in natural product synthesis. The pheromone of the beet armyworm *spodoptera exigua*, (9*Z*,12*Z*)-tetradeca-9,12-dien-1-yl acetate (**165**), was chosen as target molecule. For the final isomerization step, Ni(dppe)Cl_2 emerged as the pre-catalyst of choice. Scheme 132 summarizes the pheromone synthesis.



Scheme 132: Nickel-catalyzed *Z*-selective isomerization as key step in the total synthesis of (9*Z*,12*Z*)-tetradeca-9,12-dien-1-yl acetate (**165**).

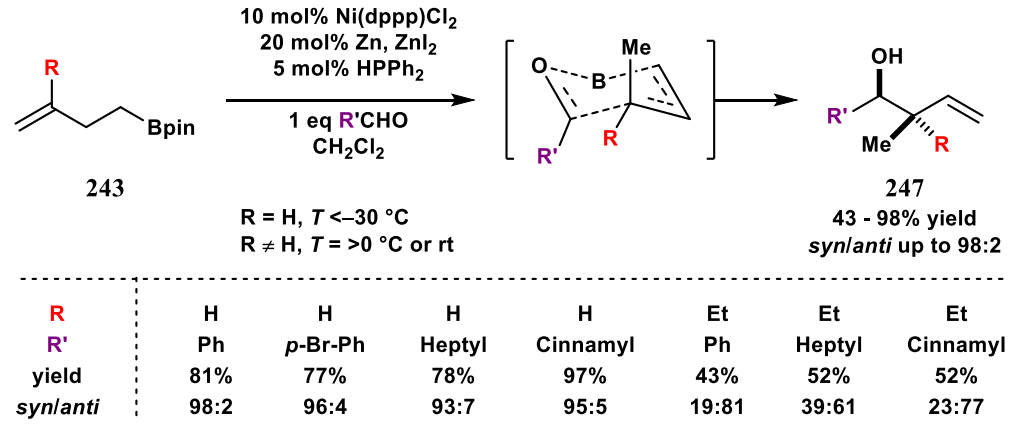
Regarding the diversification of the substrate scope, secondary and tertiary *N*-allyl amides and carbamates were well-tolerated by the catalyst.[123] Further, the nickel catalyst acted superior to the similar cobalt catalyst, which barely tolerated starting materials with a free NH-group.[33]



Scheme 133: Substrate-dependence of the nickel-catalyzed isomerization of the terminal double bond in secondary and tertiary *N*-allyl amides (X = CH_2) and carbamates (X = O).

The feature of the method was a substrate-specific isomerization. Secondary amides (and carbamates) predominantly formed the *Z*-configured enamide (and enecarbamate, respectively) with *Z*-isomeric excesses of up to 86%, whereas tertiary amides and oxazolidinones gave the *E*-configured product.[123]

The final challenge of the catalyst system was the tolerance towards functional groups, which were not located in the substrate itself, but additional reactants. This would allow an application in a one-pot multicomponent reaction sequence.



R	H	H	H	H	Et	Et	Et
R'	Ph	*p*-Br-Ph	Heptyl	Cinnamyl	Ph	Heptyl	Cinnamyl
yield	81%	77%	78%	97%	43%	52%	52%
syn/*anti*	98:2	96:4	93:7	95:5	19:81	39:61	23:77

Scheme 134: Nickel-catalyzed diastereoselective isomerization/allylboration sequence.

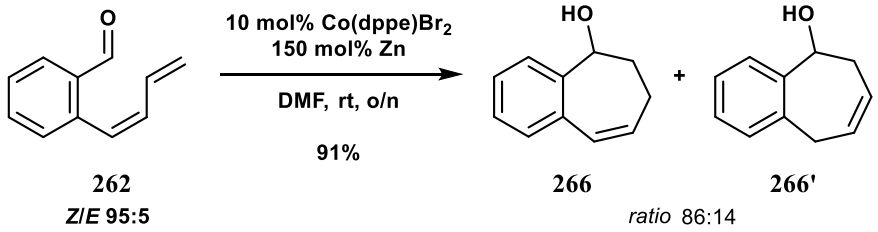
In the course of this work, an isomerization/allylboration sequence was realized. Homoallyl pinacol boronic esters of type **243** could be isomerized to their crotyl species in the presence of an aldehyde R'CHO, which then underwent an *in situ* allylboration at adjusted reaction temperature. In the sequence with unfunctionalized homoallyl boronic esters **132** (R = H) *syn*-diastereomeric excesses of up to 96% were obtained. Through utilization of substituted boronic esters with an *exo*-double bond (R = Alkyl, Ph, ≠ H), the corresponding *anti*-configured product

could be obtained in *anti*/*syn* ratios of up to 81:19.[125] Scheme 51 gives an overview of selected substrate combinations.

On the basis of mechanistic investigations, the isomerization of a broad substrate scope and the application in natural product synthesis as well as a one-pot sequence, the cobalt and nickel-catalyzed *Z*-selective isomerization of terminal alkenes could be successfully elaborated and finalized.

4.2 Cobalt-catalyzed Intramolecular Reductive Cyclization of 1,3-Dienes

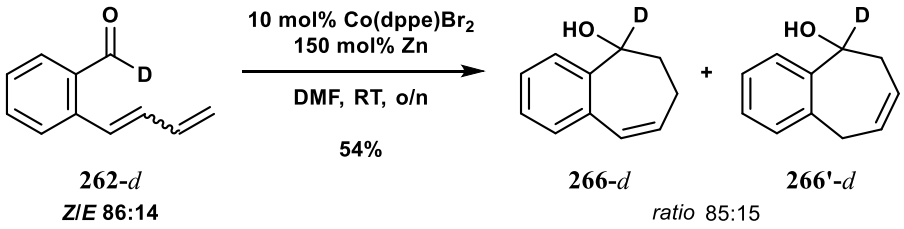
A cobalt-catalyzed reductive cyclization of 1,3-dienes could be realized by using the established cobalt catalyst Co(dppe)Br_2 and stoichiometric amounts of Zn for the synthesis of phenylazepanol derivatives **266**.



Scheme 135: Cobalt-catalyzed reductive cyclization of (*Z*)-2-(buta-1,3-dien-1-yl)benzaldehyde (**262**).

It is important to use pure *Z*-configured starting material, since the *E*-isomer solely undergoes a Zn-mediated reduction to the corresponding benzyl alcohol without the desired cyclization.

The terminal double bond of the 1,3-diene moiety reacted as nucleophile, probably in the manner of a Prins reaction. Deuteration experiments conclude that the formyl hydrogen atom did not undergo a β-hydride elimination. In the product, the deuterium atom remained at its original position (see Scheme 136). The protons must be donated from traces of water in the solvent, since deuterons from DMF-d_7 were not incorporated in the product, as well.



Scheme 136: Reductive cyclization of **262**-*d*. The deuterium atom remains in benzylic position.

In future studies, the origin of the protons as well as a potential existence of a Co–H species shall be clarified. Furthermore, the substrate scope of the method shall be extended to get diastereoselective access to different seven-membered ring structures through variation of the alk(en)yl substituents as shown in Figure 22.

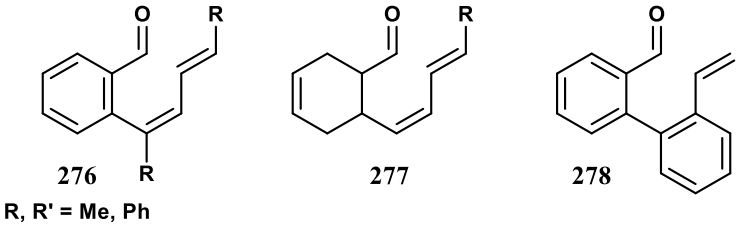
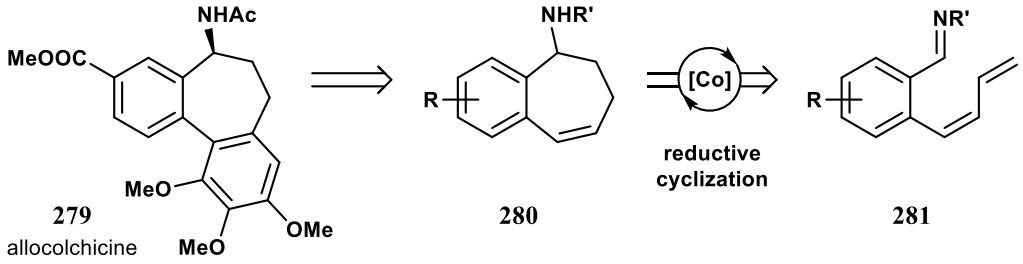


Figure 22: Possible substrates for the cobalt-catalyzed reductive cyclization.

In addition to the synthesis of benzylic alcohols, a cyclization of 1,3-dienes with an imine moiety could be an attractive approach for a potential application in natural product synthesis. The structure motif of cycloheptanamines can be found in the natural product class of the allocolchicinoids (**279** in Scheme 137), which show potential as anti-cancer drugs.[133]



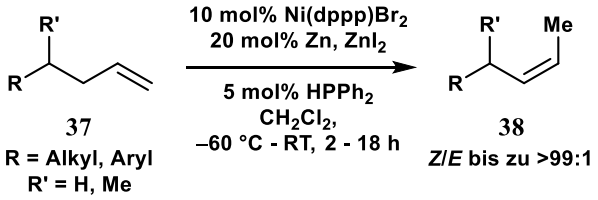
Scheme 137: Allocolchicine and potential retrosynthetic approach.

In this dissertation, first investigations concerning the cobalt-catalyzed reductive cyclization of 1,3-dienes were performed. The reaction is still a part of ongoing research in the Hilt group.

4. Zusammenfassung und Ausblick

4.1 Nickel-katalysierte *Z*-selektive Isomerisierung terminaler Alkene

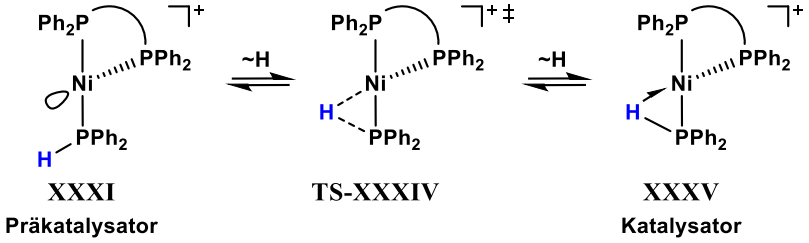
Im Rahmen der vorliegenden Dissertation konnte der Mechanismus der Nickel-katalysierten *Z*-selektiven Isomerisierung terminaler Alkene mit dem Additiv Diphenylphosphin aufgeklärt werden.



Schema 138: Nickel-katalysierte Isomerisierung terminaler Alkene.

Ein Nachweis der postulierten aktiven Nickel(I)- und Cobalt(I)-Spezies erfolgte durch cyclovoltammetrische Messungen. Des Weiteren konnte qualitativ die Existenz einer Nickel(I)-Spezies durch EPR-Experimente bestätigt werden.[103]

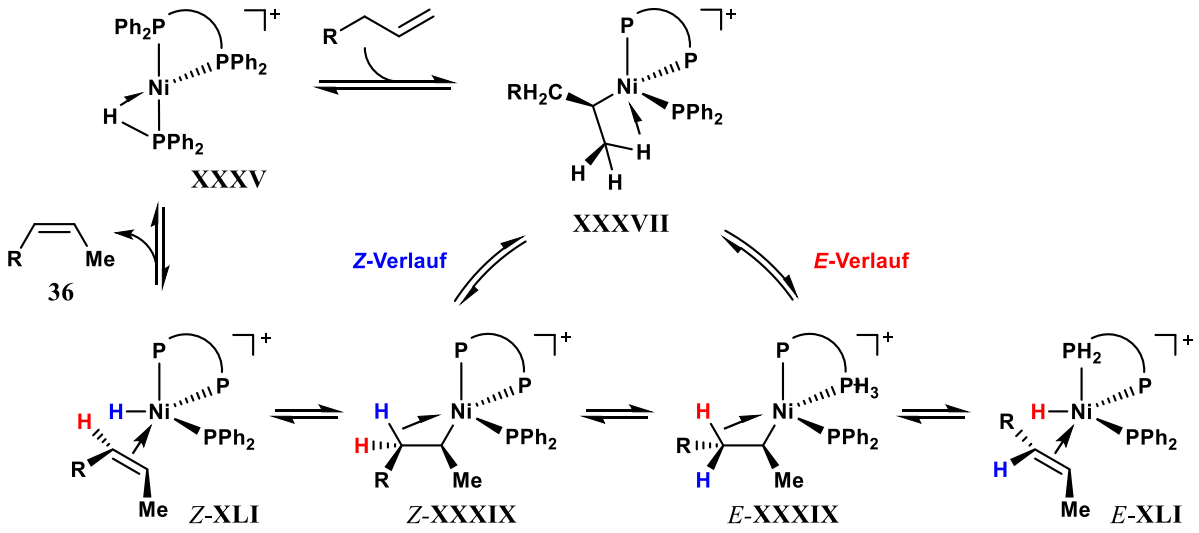
Die Rolle des Additivs $HPPh_2$ konnte in Kooperation mit Evgeny I. Grigoryev und Prof. Dr. Robert Berger durch DFT-Rechnungen enthüllt werden. Die Berechnungen kommen zu dem Ergebnis, dass das Wasserstoff-Atom direkt vom Co-Liganden auf das Substrat übertragen wird, um den Isomerisierungsprozess einzuleiten. Im Alkylmechanismus konnte die Aktivierung des Präkatalysators **XXXI** über einen dreigliedrigen Überganszustand **TS-XXXIV** beschrieben werden. Die aktive Katalysatorspezies **XXXV** ist über eine α-agostische Wechselwirkung stabilisiert, bei der die Ni–H Bindungsordnung bei 0.3 liegt und jene für P–H bei 0.6 (Schema 139).[110]



Schema 139: Bildung der aktiven Nickelkatalysator-Spezies **XXXV**.

Die *Z*-Selektivität der Isomerisierung ließ sich auf den finalen Schritt, die β-Hydrid-Eliminierung, zurückführen, die aus dem β-agostischen Komplex **XXXIX** erfolgt, in dem die Methylgruppe und Rest R *syn*-artig zueinanderstehen. Daraus entsteht die *Z*-Konfiguration der resultierenden internen Doppelbindung. Die aktive Katalysatorspezies **XXXV** wird nach

Freisetzung des 2-Alkens **36** zurückgebildet. Berechnete und experimentelle Werte der *Z*/*E*-Verhältnisse ausgewählter Isomerisierungsprodukte waren hierbei in guter Übereinstimmung miteinander.[110]

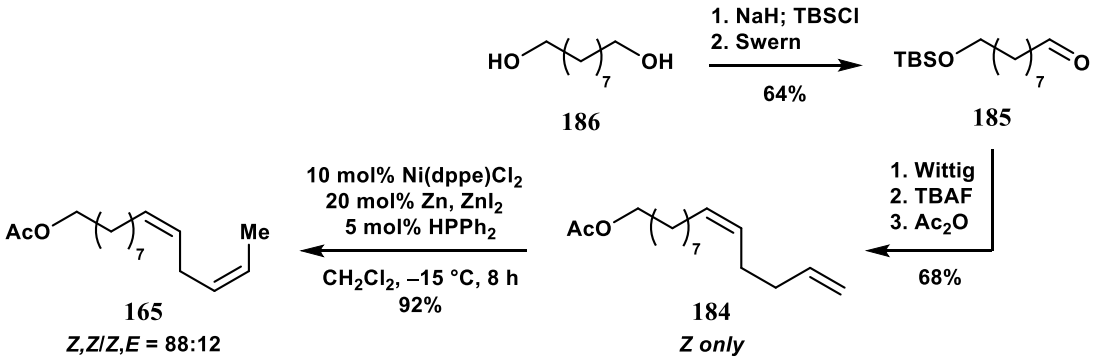


Schema 140: *β*-Hydrid-Eliminierung als selektivitätsbestimmender Schritt im berechneten Alkyl-Mechanismus.

Da die Isomerisierung von Allylbenzol-Derivaten stets *E*-selektiv ablief, wurde der Reaktionsablauf über einen *π*-Allylmechanismus (siehe Kapitel 1.1.1) durch DFT-Rechnungen vorhergesagt und konnte durch Deuterierungsexperimente untermauert werden.

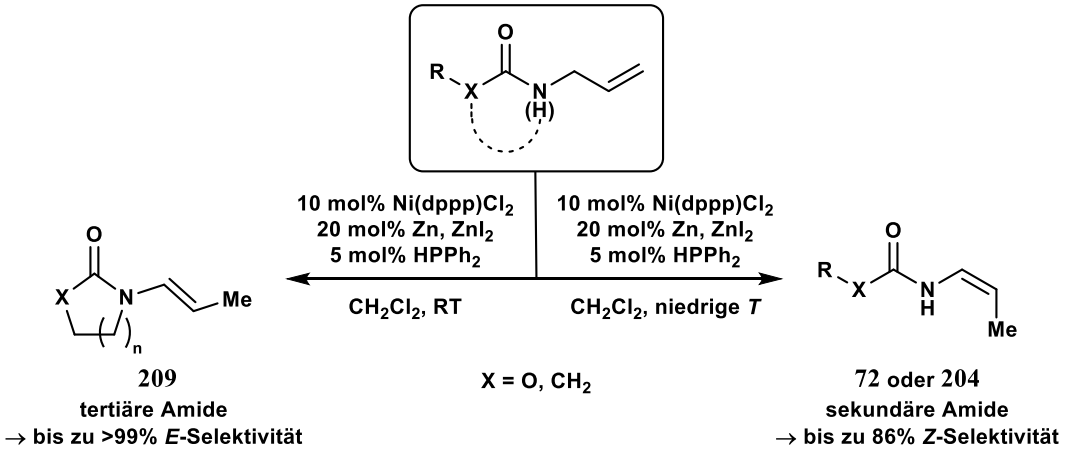
Die Nickel-katalysierte *Z*-selektive Isomerisierung terminaler Alkene konnte erfolgreich als Schlüsselschritt in der Naturstoffsynthese eingesetzt werden. Als Zielmolekül diente das Pheromon des Eulenfalters *spodoptera exigua*, (9*Z*,12*Z*)-Tetradeca-9,12-dien-1-ylacetat (**165**).

Der finale Isomerisierungsschritt gelang bei einer substratspezifisch angepassten Reaktionstemperatur von −15 °C und 8 h Reaktionszeit. $Ni(dppe)Cl_2$ stellte sich als effektivster Katalysatorvorläufer heraus. Schema 141 fasst die gesamte Pheromon-Synthese zusammen.[103]



Schema 141: Nickel-katalysierte *Z*-selektive Isomerisierung als Schlüsselschritt in der Totalsynthese von (9*Z*,12*Z*)-Tetradeca-9,12-dien-1-ylacetat (**165**).

Bezüglich der Erweiterung der Substratbreite, wurden sekundäre sowie tertiäre *N*-Allylamide und -carbamate als vom Katalysator tolerierte stickstoffhaltige Substrate ausfindig gemacht.[123] Die Nickel-katalysierte Variante der Isomerisierung war hier dem üblichen Hilt'schen Cobalt-Katalysator deutlich überlegen, da dieser Substrate mit freier NH-Funktion unzureichend bis gar nicht umsetzte.[33]

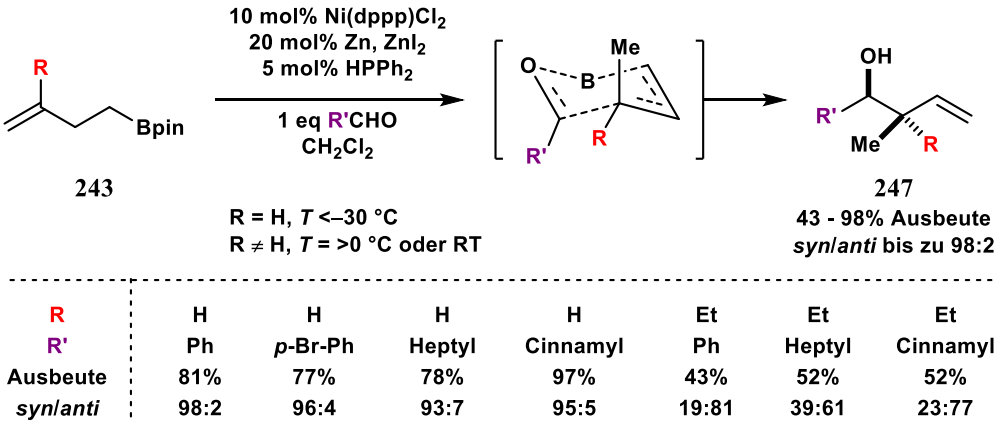


Schema 142: Substratabhängigkeit der Nickel-katalysierten Isomerisierung der terminalen Doppelbindung in sekundären und tertiären *N*-Allylamiden (X = CH_2) und -carbamaten (X = O).

Die Besonderheit der Methode bestand darin, dass die Regioselektivität der Isomerisierung substratspezifisch gesteuert wurde. Bei sekundären Vertretern der Substratklasse wurde meist bevorzugt das *Z*-konfigurierte Produkt mit einem Isomerenüberschuss von bis zu 86% gebildet, während bei cyclischen *N*-Allyllactamen und -carbamaten hauptsächlich das *E*-konfigurierte Enlactam bzw. Encarbamat gebildet wurde.[123]

Die finale Herausforderung der Methode war die Toleranz gegenüber funktionellen Gruppen, die nicht im zu isomerisierenden Substrat, sondern weiteren Reaktanden, enthalten sind. Dies ließe eine Anwendung in Mehrkomponentenreaktionen im Eintopfverfahren zu.

Im Rahmen dieser Arbeit konnte eine Isomerisierungs/Allylborierungs-Sequenz realisiert werden, bei der Homoallylboronsäurepinacolester vom Typ **243** in Gegenwart funktionalisierter Aldehyde R'CHO bei angepasster Reaktionstemperatur zunächst zur Crotylbor-Spezies isomerisiert werden, um *in situ* eine Allylborierung zu unterlaufen. Schema 143 gibt einen Überblick.[125]



R	H	H	H	H	Et	Et	Et
R'	Ph	*p*-Br-Ph	Heptyl	Cinnamyl	Ph	Heptyl	Cinnamyl
Ausbeute	81%	77%	78%	97%	43%	52%	52%
syn/*anti*	98:2	96:4	93:7	95:5	19:81	39:61	23:77

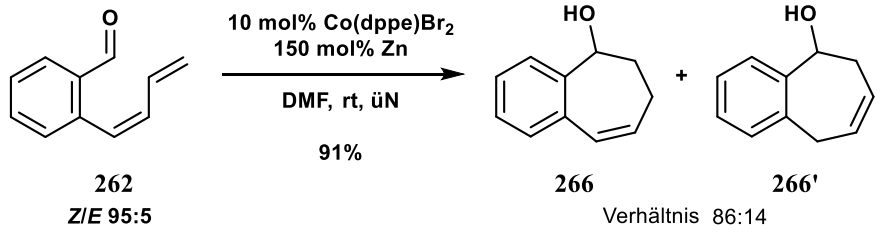
Schema 143: Nickel-katalysierte diastereoselektive Isomerisierungs/Allylborierungs-Sequenz.

Bei der Sequenz mit linearen Alkenyl-Homoallylboronsäureestern (**132**, R = H) konnten *syn*-Diastereomerenüberschüsse von bis zu 96% erhalten werden. Wurden Substrate, die eine *exo*-Doppelbindung aufwiesen (R = Alkyl, Ph; ≠ H), eingesetzt, konnte das entsprechende *anti*-konfigurierte Produkt in einem *anti*/*syn*-Verhältnis von bis zu 81:19 erhalten werden.[125]

Auf Grundlage mechanistischer Untersuchungen, der Erweiterung der Substratbreite sowie der Anwendung der Methode in der Naturstoffsynthese und im Eintopfverfahren konnte das Themenfeld der Cobalt- und Nickel-katalysierten *Z*-selektiven Monoisomerisierung terminaler Olefine in dieser Arbeit erfolgreich ausgearbeitet werden.

4.2 Cobalt-katalysierte intramolekulare reduktive Zyklisierung von 1,3-Dienen

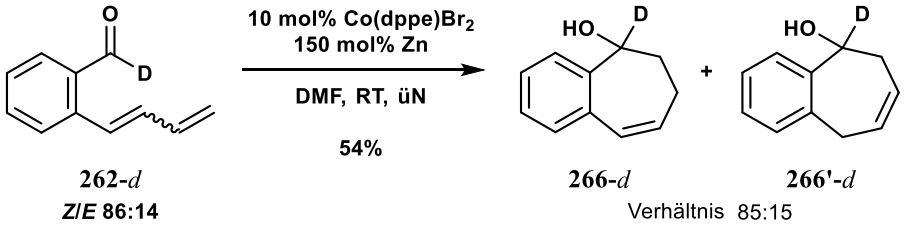
Weiterhin konnte im Rahmen dieser Arbeit eine Cobalt-katalysierte intramolekulare reduktive Zyklisierung von 1,3-Dienen realisiert werden. Unter Verwendung des in der eigenen Gruppe etablierten Cobalt-Katalysators Co(dppe)Br_2 und stöchiometrischen Mengen Zink gelang die Synthese von Dihydrobenzoannulenol-Derivaten (**266**).



Schema 144: Cobalt-katalysierte reduktive Zyklisierung von (*Z*)-2-(Buta-1,3-dien-1-yl)benzaldehyd (**262**).

Bei der Reaktionsführung war wichtig, dass rein *Z*-konfiguriertes 1,3-Dien **262** eingesetzt wurde, da das entsprechende *E*-Isomer durch Zink lediglich reduziert wurde, ohne eine Zyklisierung zu unterlaufen.

Die terminale Doppelbindung der 1,3-Dien Einheit reagierte formal als Nucleophil, womöglich nach Art einer Prins Reaktion. Deuterierungsexperimente legten den Schluss nahe, dass das formylische Wasserstoff-Atom keine β-Hydrid-Eliminierung durchlief, da es im Produkt an seiner ursprünglichen Stelle wiederzufinden (siehe Schema 145) war. Die Protonen stammen womöglich aus Spuren von Wasser im Lösungsmittel DMF, da sie auch nicht aus DMF selbst eingebaut wurden.



Schema 145: Reduktive Zyklisierung von **262**-*d* mit Verbleib des Deuterium-Atoms an benzylischer Position im Produkt.

In fortlaufenden Studien soll der Ursprung der Protonen sowie die Existenz einer Co–H-Spezies noch weiter aufgeklärt werden. Zudem soll die Substratbreite dieser Methode ausgedehnt werden, um den diastereoselektiven Zugang zu verschieden substituierten Siebenringen zu ermöglichen. Zudem kann das Rückgrat durch die Verwendung anderer Alk(en)yl-Ringe variiert werden, wie Abbildung 23 verdeutlicht.

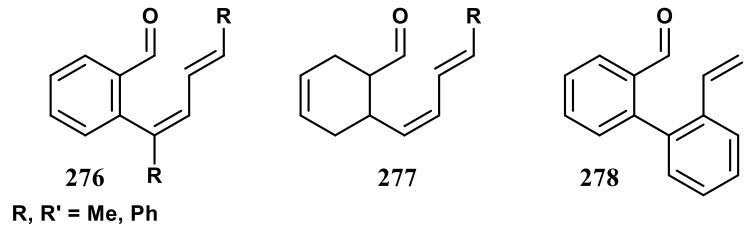
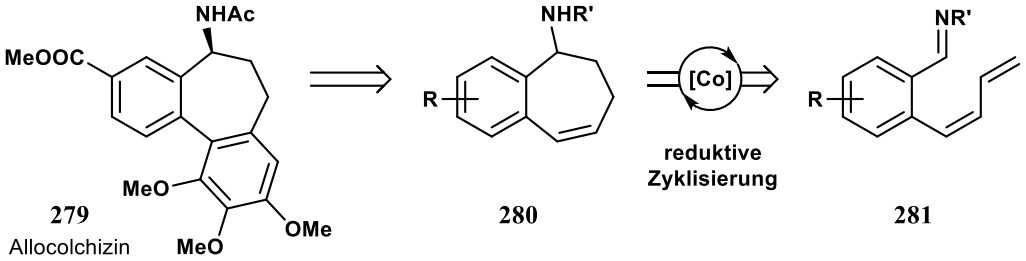


Abbildung 23: Mögliche Substrate für die Cobalt-katalysierte reduktive Zyklisierung.

Neben dem bisherigen Zugang zu benzylischen Alkoholen wäre auch die Zyklisierung von 1,3-Dienen an eine Imin-Funktion für eine potentielle Anwendung in der Naturstoffsynthese erstrebenswert. Das Strukturmotiv des Cycloheptanamids findet sich in der Naturstoffklasse der Allocolchizinoide wider (**279** in Schema 146), welche als potentielle Wirkstoffe Anwendung finden könnten.[133]



Schema 146: Allocolchizin und möglicher retrosynthetischer Zugang.

Im Rahmen dieser Dissertation wurden erste Untersuchungen zur Cobalt-katalysierten reduktiven Zyklisierung von 1,3-Dienen angestellt. Die Reaktion gehört zu den aktuellen Forschungsthemen in der eigenen Gruppe.

5. Experimental Section

5.1 Materials and Analytical Methods

Nuclear Magnetic Resonance (NMR)

1H, ^{2}H and ^{13}C spectra were either recorded on a Bruker AV III HD 300 (300 MHz for ^{1}H, 46 MHz for ^{2}H, and 75 MHz for ^{13}C), a Bruker DRX-500 or a Bruker AV III HD 500 (500 MHz for ^{1}H, 77 MHz for ^{2}H, and 125 MHz for ^{13}C). Chemical shifts are reported in parts per million (ppm) and are referenced to the solvent peak as internal standard ($CHCl_3$: δ = 7.26 ppm for ^{1}H NMR, $CDCl_3$: δ = 7.26 ppm for ^{2}H NMR, and 77.16 ppm for ^{13}C NMR, C_6H_6: 7.16 ppm for ^{1}H NMR and 128.06 ppm for ^{13}C, DMSO: 2.50 ppm for ^{1}H NMR and 39.52 ppm for ^{13}C, THF: 1.72, 3.58 ppm for ^{1}H NMR and 25.31, 67.21 ppm for ^{13}C NMR). ^{19}F and ^{11}B NMR spectroscopic data were recorded on a Bruker AV III HD 300 (121 MHz for ^{31}P, 283 MHz for ^{19}F and 96 MHz for ^{11}B) and are referenced to the external standards CCl_3F (δ = 0.00 ppm for ^{19}F) and $BF_3{\cdot}OEt_2$ (δ = 0.00 ppm for ^{11}B). ^{31}P NMR spectroscopic data were either recorded on a Bruker DRX-250 (101 MHz) or a Bruker AV III HD 300 (121 MHz) and are referenced to the external standard H_3PO_4 (85%, δ = 0.00 ppm). All NMR spectroscopic data were recorded at ambient temperature.

The multiplicity of the signals is described by the following abbreviations: s (singlet), d (dublet), t (triplet), q (quartett), quin (quintett), sept (septet), m (multiplet) and p (pseudo signal, e.g. pd = pseudo-dublet).

Infrared Spectroscopy (IR)

IR spectra were recorded on a Bruker IFS 88 fourier transform infrared spectrometer (FTIR). Absorption bands ν are given in wavenumbers (cm^{-1}).

Gaschromatography (GC and GC/MS)

GC analysis was performed on a Shimadzu GC-2010 Plus series gas chromatograph with a flame ionization detector (FID). GC/MS spectra were either recorded on an Agilent 6890 gas chromatograph coupled with a Hewlett Packard 5973 mass selective detector or a Shimadzu GC-2010 Plus gas chromatograph coupled with a Shimadzu GCMS-QP2020 mass selective detector. Helium was used as carrier gas on a Macherey Nagel Optima 5 HT column (30 m, 0.25 mm ID, 0.25 μm film).

High Resolution Mass Spectrometry (HRMS)

EI-HRMS spectra were recorded on a Finnigan MAT 95S mass spectrometer at an energy of 70 eV. ESI-HRMS spectra were recorded on a Thermo Fisher Scientific LTQ-FT mass spectrometer.

Thin Layer Chromatography and Flash Chromatography (TLC and FC)

Flash chromatography was carried out on Macherey-Nagel Silica 60 (40-63 μm, 230-400 mesh ASTM). Thin layer chromatography was carried out on Merck TLC plates (Silica 60, F254 with fluorescence indicator).

Cyclic Voltammetry

Cyclic voltammetry was carried out on a BAS C3 Cell Strand and a BAS 100 series electrochemical analyzer using a platinum disk working electrode (2.0 mm diameter) and a platinum wire counter electrode (0.5 mm diameter) at ambient temperature in CH_2Cl_2 containing Bu_4NBF_4 (0.1 M). Potentials were referred to a saturated Ag/AgCl (3.0 M NaCl) reference electrode. Before each experiment, the surface of the working electrode was polished followed by thorough rinsing with distilled water and the solution was purged with nitrogen.

EPR Spectroscopy

EPR spectra were recorded on a Bruker ESP 300 EPR spectrometer operating in the X-band with a microwave frequency of 9.1 – 9.3 GHz and a microwave power of 0.32 mW. The spectrometer is equipped with a standard variable temperature set up, a suitable data station for the storage and manipulation of the EPR spectra, an NMR gaussmeter for calibration of the magnetic field and a microwave frequency counter for the determination of the g-factors that were corrected with respect to that of the external standard DPPH (2,2-diphenyl-1-picrylhydrazyl, g = 2.0037).

Solvents and Chemicals

Dichloromethane was dried over calcium hydride and diethyl ether (Et_2O) and tetrahydrofuran (THF) over sodium under nitrogen atmosphere. All solvents were distilled under nitrogen atmosphere and stored over molecular sieves (4 Å). HPLC grade acetonitrile, toluene and DMF were further dried over molecular sieves (4 Å) and stored under nitrogen atmosphere. All reagents were used as purchased from commercial suppliers (Sigma Aldrich, Alfa Aesar, TCI, Chempur, abcr, Acros) without further purification or were prepared according to literature-

known procedures. Zinc iodide was purchased from Acros and dried *in vacuo* at 180 °C for 24 h.

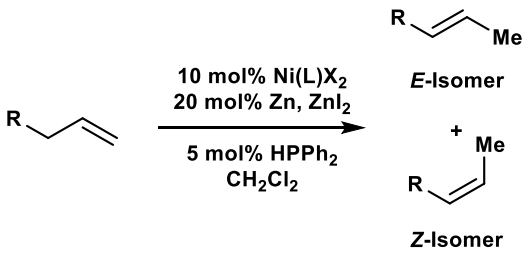
Nickel(II) and Cobalt(II) complexes were synthesized by treatment of the corresponding metal halide (1.0 eq) and ligand (1.0 eq) in anhydrous THF (0.1 M) at ambient temperature overnight. By addition of *n*-pentane, the catalyst was precipitated, filtered, dried, and used without further purification or characterization.

General Operational Methods

All experiments with water or air-sensitive reagents were carried out utilizing standard Schlenk techniques under argon atmosphere. The determination of yields was carried out gravimetrically. The stated values are in weight-% relative to the quantities of the starting material. In case of volatile products, the content of solvent residues was evaluated by ^{1}H NMR-analysis and considered when determining the yield.

5.2 General Procedures

GP 1: General Procedure for the Nickel-Catalyzed Isomerization of 1-Alkenes to 2-Alkenes

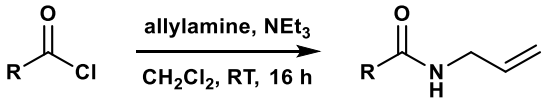


Under argon atmosphere, 10 mol% of the nickel catalyst (50.0 μmol), 20 mol% zinc powder and anhydrous zinc iodide (100 μmol) are suspended in 0.3 mL anhydrous dichloromethane in a heat gun dried Schlenk tube fitted with a Teflon® screwcap. The mixture is stirred for 10 min. Then, 0.2 mL of a $HPPh_2$ solution (25.0 μmol, 5.0 mol%, 0.125 M in dichloromethane) are added. After stirring for additional 10 min the mixture is cooled to the stated temperature and 0.50 mmol of the 1-alkene (1.0 eq) are added.

The reaction progress is monitored by GC and/or GC/MS analysis. By addition of *n*-pentane the reaction is stopped at the point where a further conversion lowers the excess of the *Z*-configured isomer. The general workup contains filtering through a short pad of silica gel with *n*-pentane or *n*-pentane/Et_2O as eluent, removal of the solvent and purification of the crude product by FC on silica gel. The conversion, as well as the *E*/*Z* ratio is determined by integration

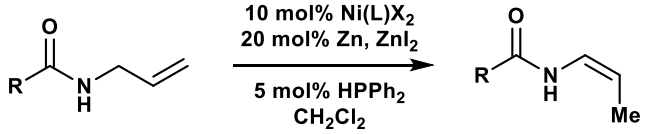
of suitable baseline separated ^{1}H NMR signals. The content of other isomers is determined by integration of baseline separated gas chromatogram peaks.

GP 2: General Procedure for the Preparation of *N*-Allyl Amides



According to a procedure of Staubitz[122] under argon atmosphere, allylamine (1.0 eq) and triethylamine (1.0 eq) are dissolved in anhydrous dichloromethane (1.0 M) and a solution of the corresponding acid chloride (1.0 eq) in anhydrous dichloromethane (2.5 M) is added at 0 °C. After stirring overnight at ambient temperature, the reaction mixture is quenched with H_2O, followed by extraction with dichloromethane. The crude product is purified by FC (*n*-pentane/EtOAc or *n*-pentane/Et_2O) or recrystallization.

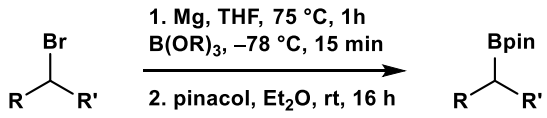
GP 3: General Procedure for the Isomerization of *N*-Allylamides and *N*/*O*-Allylcarbamates



Under argon atmosphere, 10 mol% of the nickel catalyst (50.0 μmol), 20 mol% zinc powder and anhydrous zinc iodide (100 μmol each) are suspended in either 0.3 mL anhydrous dichloromethane or 0.3 mL anhydrous acetonitrile in a heat gun dried Schlenk tube fitted with a Teflon® screwcap. The mixture is stirred for 10 min and 0.2 mL of a $HPPh_2$ solution (25.0 μmol, 5.0 mol%, 0.125 m in dichloromethane or acetonitrile) are added. After stirring for additional 10 min the mixture is cooled to the stated temperature. Then, 0.50 mmol of the corresponding *N*-allylamide or *N*/*O*-allylcarbamate (1.0 eq) are added and the reaction is stirred at the desired temperature.

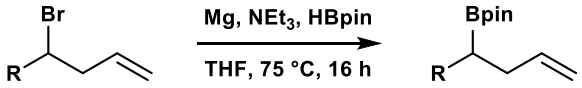
The reaction progress is monitored by GC/MS analysis. In case of incomplete conversion of the starting material another portion of catalyst is added. The reaction is stopped by addition of Et_2O, when no further conversion could be detected. The solution is directly purified by FC on silica gel (*n*-pentane/Et_2O or *n*-pentane/EtOAc). The *E*/*Z* ratio of the product is determined by integration of suitable baseline separated ^{1}H NMR signals and comparison with the corresponding peaks in the GC/MS spectrum.

GP 4: General Procedure for the Grignard Reaction with $B(OR)_3$



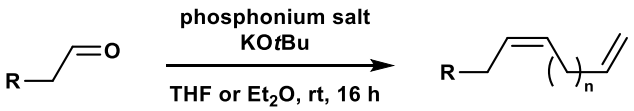
According to a procedure of Hilt[(Peters Paper)] under argon atmosphere, magnesium turnings (1.2 eq) are suspended in either anhydrous Et_2O or THF (1.0 M based on the bromide) and the corresponding bromide (1.0 eq) is added at ambient temperature. The reaction mixture is stirred at 40 °C for 1 h and then cooled to −78 °C. $B(OMe)_3$ or $B(OiPr)_3$ (1.2 eq) is added at −78 °C and the reaction mixture is stirred for 15 min at this temperature. 1 M aqueous HCl is used to quench the reaction, followed by extraction of the aqueous layer with Et_2O. After removal of the solvent the residue is taken up in the solvent mixture *n*-pentane/Et_2O (4:1) and pinacol (1.2 eq) is added. After stirring for 3 d at ambient temperature, the solvent is evaporated, and the crude product is purified by FC (*n*-pentane/Et_2O).

GP 5: General Procedure for the Grignard Reaction with Pinacolborane



According to a procedure of Duñach[1] under argon atmosphere, the corresponding bromide (1.0 eq) is added to a suspension of magnesium turnings (1.2 eq), pinacolborane (1.0 eq) and triethylamine (1.0 eq) in anhydrous THF (0.3 M) at ambient temperature. The mixture is stirred to reflux overnight. 0.1 M HCl is used to quench the reaction, followed by extraction with Et_2O. The crude product is purified by FC (*n*-pentane/Et_2O).

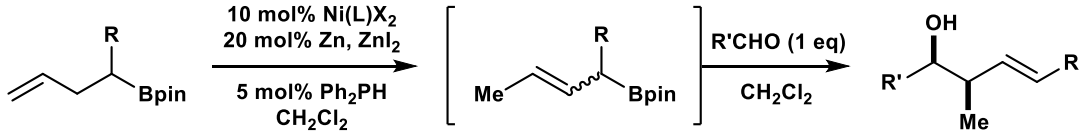
GP 6: General Procedure for the Wittig Reaction for the Preparation of Terminal Alkenes



The corresponding alkenyltriphenylphosphonium salt (1.1 – 1.5 eq) and potassium *tert*-butoxide (1.1 – 1.5 eq) are suspended in either ahydrous Et_2O or THF (0.5 M) at 0 °C under argon atmosphere. The mixture is stirred at ambient temperature for 20 – 30 min before the corresponding aldehyde or ketone (1.0 eq) is added at 0 °C. The reaction mixture is stirred overnight at ambient temperature before being quenched with saturated aqueous NH_4Cl

solution and extraction with *n*-pentane or Et_2O. The crude product is adsorbed on silica and purified by FC (pure *n*-pentane or *n*-pentane/Et_2O).

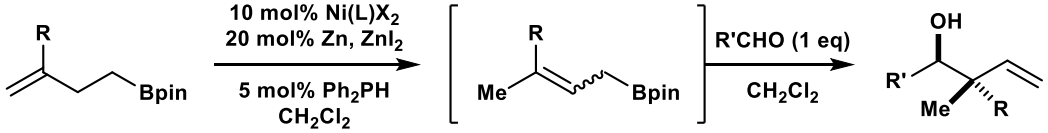
GP 7: General Procedure for the Nickel-Catalyzed Isomerization/Allylboration Sequence of Homoallylic Boronic Esters



Under argon atmosphere, 10 mol% of the nickel catalyst (either 25 or 50 μmol), 20 mol% zinc powder and anhydrous zinc iodide (either 50 or 100 μmol each) are suspended in either 0.15 or 0.3 mL anhydrous dichloromethane in a heat gun dried Schlenk tube fitted with a Teflon® screwcap. The mixture is stirred for 10 min and either 0.1 or 0.2 mL of a $HPPh_2$ solution (12.5 or 25.0 μmol, 5.0 mol%, 0.125 M in dichloromethane) are added. After stirring for additional 10 min the mixture is cooled to the stated temperature. Then, either 0.25 or 0.50 mmol of the aldehyde and the corresponding homoallylic boronic ester (1.0 eq each) are added and the reaction is stirred at the desired temperature.

The reaction progress is monitored by GC and/or GC/MS analysis. By addition of Et_2O the reaction is stopped at the point where no further conversion is detected. The general workup contains filtering through a short pad of silica gel with *n*-pentane or *n*-pentane/ Et_2O as eluent, removal of the solvent and purification of the crude product by FC on silica gel. The conversion, as well as the diastereomeric *syn*/*anti* ratio (*d.r.*) of the product are determined by integration of suitable baseline separated ^1H NMR signals.

GP 8: General Procedure for the Nickel-Catalyzed Isomerization/Allylboration Sequence of Branched Homoallylic Boronic Esters

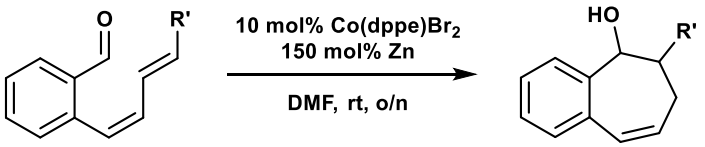


Under argon atmosphere, 10 mol% of the nickel catalyst (25 μmol), 20 mol% zinc powder and anhydrous zinc iodide (50 μmol each) are suspended in 0.15 mL anhydrous dichloromethane in a heat gun dried Schlenk tube fitted with a Teflon® screwcap. The mixture is stirred for 10 min and 0.1 mL of a $HPPh_2$ solution (12.5 μmol, 5.0 mol%, 0.125 M in dichloromethane) are added. After stirring for additional 10 min at ambient temperature 0.25 mmol of the corresponding homoallylic boronic ester (1.0 eq) are added and the reaction is stirred overnight.

After complete conversion 0.25 mmol of the aldehyde (1.0 eq) are added and the mixture was stirred for another 24 h at ambient temperature.

The reaction progress is monitored by GC and/or GC/MS analysis. By addition of Et_2O the reaction is stopped at the point where no further conversion is detected. The general workup contains filtering through a short pad of silica gel with *n*-pentane or *n*-pentane/ Et_2O as eluent, removal of the solvent and purification of the crude product by FC on silica gel. The conversion, as well as the diastereomeric *syn*/*anti* ratio (*d.r.*) of the product are determined by integration of suitable baseline separated ^1H NMR signals.

GP 9: General Procedure for the Cobalt-Catalyzed Reductive Cylization



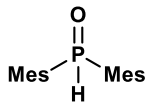
Under argon atmosphere, 10 mol% of $Co(dppp)Br_2$ (50.0 μmol) and 150 mol% zinc powder (0.75 mmol) were suspended in 1.0 mL anhydrous DMF in a heat gun dried Schlenk tube fitted with a Teflon® screwcap. The mixture was stirred for 10 min and 0.50 mmol of the corresponding 1,3-diene (1.0 eq) were added and the reaction was stirred overnight at ambient temperature, unless otherwise stated.

The reaction progress was monitored by GC/MS analysis. In case of incomplete conversion of the starting material, another portion of catalyst was added. By addition of Et_2O, the reaction was stopped when no further conversion could be detected. The solution was directly purified by FC on silica gel (*n*-pentane/Et_2O).

5.3 Isomerization of Terminal Alkenes to *Z*-2-Alkenes

5.3.1 Synthesis of Diphenylphosphine Analogues

Dimesitylphosphine oxide (174a)



According to a procedure of Busacca,[113] 0.67 g (27.5 mmol, 7.6 eq) magnesium turnings were suspended in ahydrous THF and 2.38 g (12.0 mmol, 3.3 eq) bromomesitylen and a small amount of I_2 were added. After exothermic reaction of the Grignard reagent and stirring for another hour at 75 °C 0.50 g diethyl phosphite (3.62 mmol, 1.0 eq) were added within 15 min at 0 °C and the reaction was stirred overnight at ambient temperature. Aqueous HCl (5 mL) was added at 0 °C followed by addition of MTBE. The aqueous layer was extracted three times with CH_2Cl_2 and the combined organic layers were dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure. The crude product was recrystallized from hot EtOAc to give dimesitylphosphine oxide (**174a**) in 82% yield (0.85 g, 2.97 mmol) as white solid.

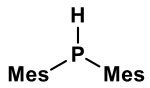
^{1}H NMR (300 MHz, $CDCl_3$) δ 8.55 (d, *J* = 476 Hz, 1H, P*H*), 6.85 (d, *J* = 3.9 Hz, 4H, CH_{ar}), 2.39 (s, 12H, *o*-CH_3), 2.28 (s, 6H, *p*-CH_3).

^{13}C NMR (75 MHz, $CDCl_3$) δ 142.0 (d, *J* = 2.5 Hz, *p*-$C_{q, ar}$), 141.9 (*d*, J = 10.7 Hz, *o*-$C_{q, ar}$), 130.6 (d, *J* = 10.6 Hz, *m*-CH_{ar}), 126.5 (d, *J* = 100.1 Hz, P$C_{q, ar}$), 21.3 (s, *p*-CH_3), 20.9 (d, *J* = 7.8 Hz, *o*-CH_3).

^{31}P NMR (121 MHz, THF-d_8) δ 10.3 (d, *J* = 475 Hz, *P*H).

The NMR spectroscopic data are in accordance with the literature.[113]

Dimesitylphosphine (175a)



According to a procedure of Busacca,[113] 500 mg dimesitylphosphine oxide (1.75 mmol, 1.0 eq) were dissolved in 8.0 mL anhydrous toluene and 12.7 mL DIBAL (1.1 M in toluene, 14.0 mmol, 8.0 eq) were added at ambient temperature. The reaction mixture was stirred at 70 °C for 24 h and then cooled to −78 °C. Degassed aqueous 2 M NaOH (10 mL) was added and the resulting suspension was warmed to ambient temperature. The lower aqueous layer was separated via syringe and the remaining organic layer was filtered over $MgSO_4$ and celite. The solvent was carefully removed in vacuo making sure that the product was not exposed to air. Dimesitylphosphine (**175a**) was obtained in 69% yield (330 mg, 1.20 mmol) as white crystalline powder and stored under argon atmosphere.

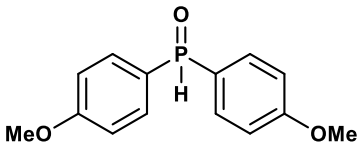
^{1}H NMR (300 MHz, C_6D_6) δ 6.69 (s, 4H, C*H*$_{ar}$), 5.32 (d, *J* = 230 Hz, 1H, P*H*), 2.27 (s, 12H, *o*-C*H*$_3$), 2.08 (s, 6H, *p*-C*H*$_3$).

^{13}C NMR (75 MHz, C_6D_6) δ 142.5 (d, *J* = 12.6 Hz, P*C*$_{q, ar}$), 137.8 (s, *p*-*C*$_{q, ar}$), 130.0 (d, *J* = 16.7 Hz, *o*-*C*$_{q, ar}$) 129.5 (d, *J* = 2.8 Hz, *C*H$_{ar}$), 23.0 (d, *J* = 11.6 Hz, *o*-*C*H$_3$), 21.0 (s, *p*-*C*H$_3$).

^{31}P NMR (121 MHz, C_6D_6) δ –92.8 (d, *J* = 230 Hz, *P*H).

The NMR spectroscopic data are in accordance with the literature.[113]

Bis(4-methoxyphenyl)phosphine oxide (174b)



According to a procedure of Busacca,[113] 0.92 g (38.0 mmol, 5.8 eq) magnesium turnings were suspended in THF and 3.09 g (16.5 mmol, 3.3 eq) 1-bromo-4-methoxybenzene and a small amount of I_2 were added. After exothermic reaction of the Grignard reagent 0.90 g diethyl phosphite (6.50 mmol, 1.0 eq) were added within 15 min at 0 °C and the reaction was stirred overnight at ambient temperature. Aqueous HCl (5 mL) was added at 0 °C followed by addition of MTBE. The aqueous layer was extracted three times with CH_2Cl_2 and the combined organic layers were dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure. The crude product was recrystallized from hot EtOAc to give bis(4-methoxyphenyl)phosphine oxide (**174b**) in 88% yield (1.51 g, 5.75 mmol) as white solid.

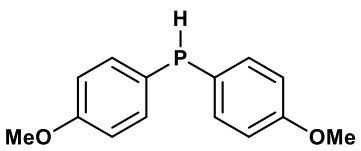
^{1}H NMR (300 MHz, $CDCl_3$) δ 8.05 (d, *J* = 459 Hz, 1H, P*H*), 7.60 (dd, *J* = 13.2, 8.7 Hz, 4H, C*H*$_{ar}$), 6.99 (dd, *J* = 8.7, 2.1 Hz, 4H, C*H*$_{ar}$), 3.84 (s, 6H, OC*H*$_3$).

^{13}C NMR (75 MHz, $CDCl_3$) δ 163.1 (*C*OCH$_3$), 132.9 (*C*H$_{ar}$), 132.7 (*C*H$_{ar}$), 114.7 (d, *J* = 10.0 Hz, P*C*$_{q, ar}$), 114.5 (P*C*$_{q, ar}$), 55.5 (O*C*H$_3$).

^{31}P NMR (121 MHz, THF-d_8) δ 20.9 ((quin)d, *J* = 477.2, 13.2 Hz, *P*H).

The NMR spectroscopic data are in accordance with the literature.[113]

Bis(4-methoxyphenyl)phosphine (175b)



According to a procedure of Busacca,[113] 1.51 g bis(4-methoxyphenyl)phosphine oxide (5.75 mmol, 1.0 eq) were dissolved in 30 mL anhydrous THF and 28.8 mL DIBAL (1.0 M in cyclohexane, 28.8 mmol, 5.0 eq) were added at ambient temperature. The reaction mixture was stirred at ambient temperature for 15 min and then cooled to 0 °C. Degassed MTBE

(20 mL) and degassed aqueous 2 M NaOH (10 mL) were added very carefully. After the addition of 10 mL of degassed brine solution the lower aqueous layer was separated via syringe and the remaining organic layer was filtered over $MgSO_4$. The solvent was carefully removed in vacuo making sure that the product was not exposed to air. Bis(4-methoxyphenyl)phosphine (**175b**) was obtained in 75% yield (1.06 g, 4.29 mmol) as white solid and stored under argon atmosphere.

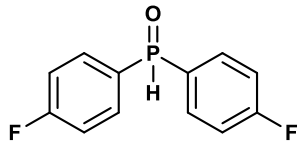
^{1}H NMR (300 MHz, C_6D_6) δ 7.39 (dd, *J* = 8.7, 6.9 Hz, 4H, C*H*$_{ar}$), 6.70 (dd, *J* = 8.7, 0.9 Hz, 4H, C*H*$_{ar}$), 5.29 (d, *J* = 214 Hz, 1H, P*H*), 3.23 (s, 6H, OC*H*$_3$).

^{13}C NMR (75 MHz, C_6D_6) δ 160.7 (s, *C*OCH$_3$), 136.0 (d, *J* = 18.3 Hz, *C*H$_{ar}$), 132.8 (d, *J* = 12.2 Hz, *C*H$_{ar}$), 126.5 (d, *J* = 8.8 Hz, *C*$_{q, ar}$), 114.7 (d, *J* = 6.8 Hz, *C*H$_{ar}$), 54.7 (O*C*H$_3$).

^{31}P NMR (121 MHz, C_6D_6) δ −44.5 ((quin)d, *J* = 215.0, 6.9 Hz, P*H*).

The NMR spectroscopic data are in accordance with the literature.[113]

Bis(4-fluorophenyl)phosphine oxide (174c)



According to a procedure of Busacca,[113] 1.38 g (56.9 mmol, 7.6 eq) magnesium turnings were suspended in anhydrous THF and 4.33 g (24.8 mmol, 3.3 eq) 1-bromo-4-fluorobenzene were added. After exothermic reaction of the Grignard reagent 1.04 g (7.50 mmol, 1.0 eq) diethyl phosphite were added within 15 min at 0 °C and the reaction was stirred overnight at ambient temperature. Aqueous HCl (5 mL) was added at 0 °C followed by addition of MTBE. The aqueous layer was extracted three times with CH_2Cl_2 and the combined organic layers were dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure. The crude product was purified by FC (EtOAc/*n*-pentane 7:3→1:0) to give bis(4-fluorophenyl)phosphine oxide (**174c**) in 90% yield (1.60 g, 6.72 mmol) as colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.09 (d, *J* = 485 Hz, 1H, P*H*), 7.75 – 7.66 (m, 4H, C*H*$_{ar}$), 7.25 – 7.18 (m, 4H, C*H*$_{ar}$).

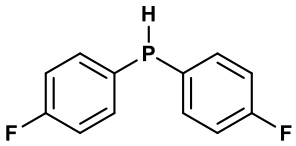
^{13}C NMR (75 MHz, $CDCl_3$) δ 133.4 (dd, *J* = 13.1, 8.9 Hz, F*C*$_{q, ar}$), 116.5 (dd, *J* = 21.5, 14.0 Hz, *C*H$_{ar}$). *C*$_{q, ar}$ not detectable.

^{19}F NMR (282 MHz, $CDCl_3$) δ −104.8.

^{31}P NMR (121 MHz, $CDCl_3$) δ 19.0 ((quin)d, *J* = 486 Hz, *P*H).

The NMR spectroscopic data are in accordance with the literature.[113]

Bis(4-fluorophenyl)phosphine (175c)



According to a procedure of Busacca,[113] 990 mg bis(4-fluorophenyl)phosphine oxide (4.14 mmol, 1.0 eq) were dissolved in 10 mL anhydrous THF and 12.4 mL DIBAL (1.0 M in cyclohexane, 12.4 mmol, 3.0 eq) were added at ambient temperature. The reaction mixture was stirred at ambient temperature for 14 h and then cooled to 0 °C. Degassed aqueous 2 M NaOH (10 mL) was added very carefully. After the addition of 10 mL of degassed brine solution and further stirring for 1 h the lower aqueous layer was separated via syringe and the remaining organic layer was filtered over $MgSO_4$. The solvent was carefully removed in vacuo making sure that the product was not exposed to air. Bis(4-fluorophenyl)phosphine (**175c**) was obtained in 49% yield (380 mg, 2.01 mmol) as white solid and stored under argon atmosphere.

^{1}H NMR (300 MHz, C_6D_6) δ 7.10 – 7.03 (m, 4H, C*H*$_{ar}$), 6.71 – 6.65 (m, 4H, C*H*$_{ar}$), 4.98 (d, *J* = 216 Hz, 1H, P*H*).

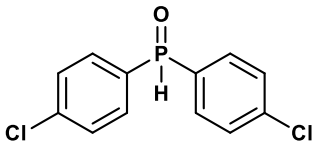
^{13}C NMR (75 MHz, C_6D_6) δ 163.8 (d, *J* = 248 Hz, F*C*$_{q, ar}$), 136.2 (dd, *J* = 18.5, 8.0 Hz, *C*H$_{ar}$), 130.5 (dd, *J* = 10.2, 3.2 Hz, P*C*$_{q, ar}$), 116.0 (dd, *J* = 20.8, 6.9 Hz, *C*H$_{ar}$).

^{19}F NMR (282 MHz, C_6D_6) δ −112.6.

^{31}P NMR (121 MHz, C_6D_6) δ −44.4 (d, *J* = 217 Hz, *P*H).

The NMR spectroscopic data are in accordance with the literature.[113]

Bis(4-chlorophenyl)phosphine oxide (174d)



According to a procedure of Busacca,[113] 1.14 g (46.9 mmol, 6.3 eq) magnesium turnings were suspended in anhydrous THF and 3.59 g (18.8 mmol, 2.5 eq) 1-bromo-4-chlorobenzene were added. After exothermic reaction of the Grignard reagent 1.04 g (7.50 mmol, 1.0 eq) diethyl phosphite were added within 15 min at 0 °C and the reaction was stirred overnight at ambient temperature. Aqueous HCl (5.0 mL) was added at 0 °C followed by addition of MTBE. The aqueous layer was extracted three times with CH_2Cl_2 and the combined organic layers were dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure. Pure bis(4-chlorophenyl)phosphine oxide (**174d**) was obtained in 50% yield (1.02 g, 3.76 mmol) as colorless oil without further purification.

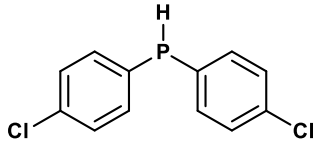
^{1}H NMR (300 MHz, $CDCl_3$) δ 8.06 (d, *J* = 486 Hz, 1H, P*H*), 7.67 – 7.58 (m, 4H, CH_{ar}), 7.52 – 7.48 (m, 4H, CH_{ar}).

^{13}C NMR (75 MHz, $CDCl_3$) δ 132.0 (d, *J* = 12.6 Hz, *C*H_{ar}), 129.5 (d, *J* = 13.8 Hz, *C*H_{ar}). $C_{q,\,ar}$ not detectable.

^{31}P NMR (121 MHz, $CDCl_3$) δ 19.0 (dt, *J* = 486, 13.4 Hz, *P*H).

The NMR spectroscopic data are in accordance with the literature.[113]

Bis(4-chlorophenyl)phosphine (175d)



According to a procedure of Busacca,[113] 1.02 g bis(4-chlorophenyl)phosphine oxide (3.76 mmol, 1.0 eq) were dissolved in 15 mL anhydrous THF and 11.3 mL DIBAL (1.0 M in cyclohexane, 11.3 mmol, 3.0 eq) were added at ambient temperature. The reaction mixture was stirred at ambient temperature for 15 min and then cooled to 0 °C. Degassed aqueous 2 M NaOH (10 mL) was added very carefully. After the addition of 10 mL of degassed brine solution and further stirring for 1 h the lower aqueous layer was separated via syringe and the remaining organic layer was filtered over $MgSO_4$. The solvent was carefully removed in vacuo making sure that the product was not exposed to air. Bis(4-chlorophenyl)phosphine (**175d**) was obtained in 35% yield (480 mg, 1.31 mmol) as white solid and stored under argon atmosphere.

^{1}H NMR (300 MHz, C_6D_6) δ 6.99 – 6.92 (m, 8H, CH_{ar}), 4.87 (d, *J* = 217 Hz, 1H, P*H*).

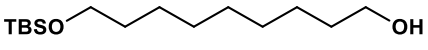
^{13}C NMR (75 MHz, C_6D_6) δ 135.5 (d, *J* = 17.7 Hz, *C*H_{ar}), 134.3 (d, *J* = 17.3 Hz, P$C_{q,\,ar}$), 133.2 (d, *J* = 11.7 Hz, $C_{q,\,ar}$), 129.0 (d, *J* = 6.6 Hz, *C*H_{ar}).

^{31}P NMR (121 MHz, C_6D_6) δ –43.4 (d, *J* = 218 Hz, 1P, *P*H).

The NMR spectroscopic data are in accordance with the literature.[113]

5.3.2 Synthesis of the Pheromone (9Z,12Z)-Tetradeca-9,12-dien-1-yl Acetate

9-((*tert*-Butyldimethylsilyl)oxy)nonan-1-ol (282)



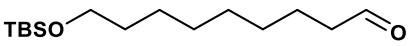
According to a procedure of Blair,[134] 1.50 g sodium hydride (60% dispersion in mineral oil, 37.5 mmol, 1.1 eq) were suspended in 250 mL anhydrous THF under argon atmosphere and 5.47 g 1,9-nonanediol (34.2 mmol, 1.0 eq) were added at ambient temperature in one portion. The mixture was stirred overnight. Then, 5.15 g TBSCl (34.2 mmol, 1.0 eq) were added in one portion at 0 °C. Stirring was continued for another 2 h. After addition of water the mixture was extracted with EtOAc. The combined organic layers were washed with brine, dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure. The crude product was purified by FC (*n*-pentane/EtOAc 2:1) to give 9-((*tert*-butyldimethylsilyl)oxy)nonan-1-ol (**282**) in 73% yield (6.82 g, 24.8 mmol) as colorless liquid.

^{1}H NMR (300 MHz, $CDCl_3$) δ 3.64 (t, *J* = 6.6 Hz, 2H, C*H*$_2$), 3.60 (t, *J* = 6.7 Hz, 2H, C*H*$_2$), 1.62 – 1.48 (m, 4H, C*H*$_2$), 1.30 (m, 11H, C*H*$_2$, O*H*), 0.89 (s, 9H, C(C*H*$_3$)$_3$), 0.04 (s, 6H, SiC*H*$_3$).

^{13}C NMR (75 MHz, $CDCl_3$) δ 63.4 (*C*H$_2$), 63.2 (*C*H$_2$), 33.0 (*C*H$_2$), 32.9 (*C*H$_2$), 29.7 (*C*H$_2$), 29.5 (*C*H$_2$), 26.1 (C(*C*H$_3$)$_3$), 25.9 (*C*H$_2$), 25.8 (*C*H$_2$), 25.7 (*C*H$_2$), 18.5 (Si*C*(CH$_3$)$_3$), −5.1 (Si*C*H$_3$).

The NMR spectroscopic data are in accordance with the literature.[135]

9-((*tert*-Butyldimethylsilyl)oxy)nonanal (283)



According to a procedure of Sammis,[136] under argon atmosphere, 6.2 mL dimethyl sulfoxide (86.4 mmol, 4.0 eq) were added to a solution of 3.69 mL oxalyl chloride (43.2 mmol, 2.0 eq) in anhydrous CH_2Cl_2 (20 mL) at −78 °C dropwise over a period of 30 min. Then a solution of 5.93 g 9-((*tert*-butyldimethylsilyl)oxy)nonan-1-ol (21.6 mmol, 1.0 eq) in 20 mL anhydrous CH_2Cl_2 was added over the same period of time and the mixture was stirred for another 90 min. Then, 24 mL triethylamine (173 mmol, 8.0 eq) were added dropwise and the resulting slurry was stirred overnight at ambient temperature. The mixture was poured into water and extracted with CH_2Cl_2, the organic layer was washed with water and brine, dried over $MgSO_4$, filtered and the solvent was removed by rotary evaporation. The crude product was purified by FC

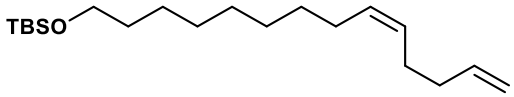
(*n*-pentane/Et_2O 5:1) to give 9-((*tert*-butyldimethylsilyl)oxy)nonanal (**283**) in 88% yield (5.19 g, 19.1 mmol) as yellow oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ 9.76 (t, *J* = 1.8 Hz, 1H, C*H*O), 3.59 (t, J = 6.6 Hz, 2H), 2.42 (dt, *J* = 7.4, 1.9 Hz, 2H, CH_2), 1.68 – 1.58 (m, 2H, CH_2), 1.55 – 1.46 (m, 2H, CH_2) 1.30 (br s, 8H, CH_2), 0.89 (s, 9H, C(CH_3)$_3$), 0.05 (s, 6H, SiCH_3).

^{13}C NMR (75 MHz, $CDCl_3$) δ 203.1 (*C*HO), 63.4 (*C*H_2), 33.8 (*C*H_2), 33.0 (*C*H_2), 29.5 (*C*H_2), 29.4 (*C*H_2), 29.3 (*C*H_2), 26.2 (C(*C*H_3)$_3$), 26.0 (*C*H_2), 22.2 (*C*H_2), 18.5 (Si*C*(CH_3)$_3$), –5.1 (Si*C*H_3).

The NMR spectroscopic data are in accordance with the literature.[137]

(*Z*)-*tert*-Butyldimethyl(tetradeca-9,13-dien-1-yloxy)silane (185)



According to a procedure of Hansson,[138] 1.75 g pent-4-enyltriphenylphosphonium bromide (4.26 mmol, 1.1 eq) in 10 mL anhydrous THF were cooled to 0 °C and 1.7 mL *n*-butyllithium (2.5 M in *n*-hexane, 4.26 mmol, 1.1 eq) were added *via* syringe. The resulting red suspension was stirred for 90 min at ambient temperature. It was then cooled to −78 °C and 1.3 mL anhydrous DMPU (10.4 mmol, 2.7 eq) were added. After 15 min 1.00 g 9-((*tert*-butyldimethylsilyl)oxy)nonanal (3.87 mmol, 1.0 eq) was added and the mixture was stirred overnight slowly warming up to ambient temperature. NH_4Cl solution was added and the solution was extracted with Et_2O, dried over $MgSO_4$, filtered and concentrated by rotary evaporation. The crude product was purified by FC (*n*-pentane/Et_2O 200:1) to give (*Z*)-*tert*-butyldimethyl(tetradeca-9,13-dien-1-yloxy)silane (**185**) in 75% (993 mg, 2.89 mmol) as colorless oil.

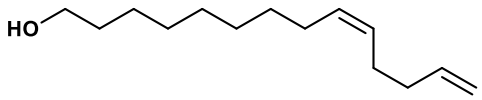
^{1}H NMR (500 MHz, $CDCl_3$) δ 5.87 – 5.79 (m, 1H, CH_{olef}), 5.41 – 5.33 (m, 2H, CH_{olef}), 5.04 – 4.95 (m, 2H, C$H_{2,\ olef}$), 3.60 (t, *J* = 6.6 Hz, 2H, CH_2), 2.15 – 2.08 (m, 4H, CH_2), 2.02 (dd, *J* = 6.9, 6.3 Hz, 2H, CH_2), 1.52 – 1.48 (m, 2H, CH_2), 1.27 (br s, 10H, CH_2), 0.89 (s, 9H, C(CH_3)$_3$), 0.05 (s, 6H, SiCH_3).

^{13}C NMR (75 MHz, $CDCl_3$) δ 138.7 (*C*H_{olef}), 130.6 (*C*H_{olef}), 129.0 (*C*H_{olef}), 114.7 (*C*$H_{2,\ olef}$), 63.5 (*C*H_2), 34.0(*C*H_2), 33.0 (*C*H_2), 29.9 (*C*H_2), 29.7 (*C*H_2), 29.6 (*C*H_2), 29.4 (*C*H_2), 27.4 (*C*H_2), 26.9 (*C*H_2), 26.2 (C(*C*H_3)$_3$), 26.0 (*C*H_2), –5.1 (Si*C*H_3). *C*(CH_3)$_3$ not detectable.

IR (neat) 3078, 3006, 2927, 2855, 1641, 1463, 1388, 1361, 1254, 1097, 1005, 993, 939, 910, 834, 812, 773, 713, 679, 661, 571, 397.

HRMS (ESI) calculated for $C_{20}H_{41}OSi^+$: *m*/*z* = 325.2921; found *m*/*z* = 325.2930.

(*Z*)-Tetradeca-9,13-dien-1-ol (284)



According to a procedure of Kalesse,[139] 5.34 mL of a TBAF solution (1.0 M in THF, 5.34 mmol, 1.2 eq) were added to a solution of 1.52 g (*Z*)-*tert*-butyldimethyl(tetradeca-9,13-dien-1-yloxy)silane (4.45 mmol, 1.0 eq) in anhydrous THF (30 mL) at 0 °C. After 1 h the reaction was quenched with water and extracted with Et_2O. The combined organic layers were washed with brine, dried over $MgSO_4$, filtered and concentrated by rotary evaporation. The crude product was purified by FC (*n*-pentane/Et_2O 5:1) to give alcohol (*Z*)-tetradeca-9,13-dien-1-ol (**284**) in 96% yield (897 mg, 4.26 mmol) as colorless oil.

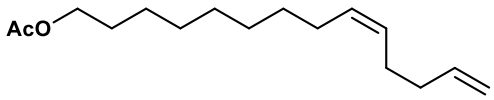
^{1}H NMR (500 MHz, $CDCl_3$) δ 5.89 – 5.76 (m, 1H, C*H*$_{olef}$), 5.43 – 5.31 (m, 2H, C*H*$_{olef}$), 5.05 – 4.94 (m, 2H, C*H*$_{2,olef}$), 3.64 (dd, *J* = 10.8, 6.4 Hz, 2H, C*H*$_2$), 2.16 – 2.09 (m, 4H, C*H*$_2$), 2.07 – 1.99 (m, 2H, C*H*$_2$), 1.60 – 1.52 (m, 2H, C*H*$_2$), 1.30 (br s, 10H, C*H*$_2$), 1.21 (br s, 1H, O*H*).

^{13}C NMR (75 MHz, $CDCl_3$) δ 138.7 (*C*H$_{olef}$), 130.6 (*C*H$_{olef}$), 129.0 (*C*H$_{olef}$), 114.7 (*C*H$_{2,\ olef}$), 63.2 (*C*H$_2$), 34.0 (*C*H$_2$), 33.0 (*C*H$_2$), 29.8 (*C*H$_2$), 29.6 (*C*H$_2$), 29.5 (*C*H$_2$), 29.4 (*C*H$_2$), 27.4 (*C*H$_2$), 26.8 (*C*H$_2$), 25.9 (*C*H$_2$).

IR (neat) 3327, 3078, 3006, 2924, 2854, 1641, 1456, 1371, 1055, 993, 910, 721, 640, 460, 382.

HRMS (EI) calculated for $C_{14}H_{26}O$: *m*/*z* = 210.1984; found *m*/*z* = 210.1999.

(*Z*)-Tetradeca-9,13-dien-1-yl Acetate (184)



According to a procedure of Jamison,[140] 1.43 mL triethylamine (10.29 mmol, 3.0 eq), 0.49 mL acetic anhydride (5.15 mmol, 1.5 eq) and 41.7 mg DMAP (0.34 mmol, 10 mol%) were added to a solution of 722 mg (*Z*)-tetradeca-9,13-dien-1-ol (3.43 mmol, 1.0 eq) in 7.0 mL anhydrous CH_2Cl_2 at 0 °C. The mixture was stirred for 2 h at ambient temperature, then quenched with NH_4Cl solution and extracted with Et_2O. The combined organic layers were washed with $NaHCO_3$ and NH_4Cl solution, water and brine, dried over $MgSO_4$, filtered and the solvent was evaporated. The crude product was purified by FC (*n*-pentane/Et_2O 15:1) to give (*Z*)-tetradeca-9,13-dien-1-yl acetate (**184**) in 95% yield (819 mg, 3.24 mmol) as colorless oil.

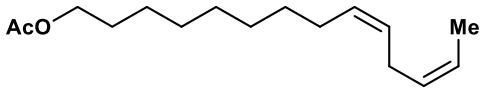
^{1}H NMR (500 MHz, $CDCl_3$) δ 5.89 – 5.76 (m, 1H, C*H*$_{olef}$), 5.43 – 5.31 (m, 2H, C*H*$_{olef}$), 5.05 – 4.93 (m, 2H, C*H*$_{2,\ olef}$), 4.05 (t, *J* = 6.8 Hz, 2H, C*H*$_2$), 2.16 – 2.09 (m, 4H, C*H*$_2$), 2.07 – 1.99 (m, 2H, C*H*$_2$), 2.04 (s, 3H, C*H*$_3$), 1.66 – 1.57 (m, 2H, C*H*$_2$), 1.30 (br s, 10 H, C*H*$_2$).

^{13}C NMR (125 MHz, $CDCl_3$) δ 171.3 (*C*=O), 138.7 (*C*H_{olef}), 130.6 (*C*H_{olef}), 129.0 (*C*H_{olef}), 114.7 (*C*$H_{2,\ olef}$), 64.8 (*C*H_2), 34.0 (*C*H_2), 29.8 (*C*H_2), 29.5 (*C*H_2), 29.4 (*C*H_2), 29.3 (*C*H_2), 28.8 (*C*H_2), 27.4 (*C*H_2), 26.9 (*C*H_2), 26.1 (*C*H_2), 21.1 (*C*H_3).

IR (neat) 3078, 3006, 2926, 2855, 1740, 1640, 1456, 1387, 1365, 1233, 1036, 994, 910, 723, 635, 606, 428.

HRMS (EI) calculated for $C_{16}H_{28}O_2$: *m*/*z* = 252.2089; found *m*/*z* = 252.2092.

(9*Z*,12*Z*)-Tetradeca-9,12-dien-1-yl Acetate (165)



The title compound was prepared according to GP 1 utilizing 13.2 mg $Ni(dppe)Cl_2$ (25.0 μmol, 10 mol%), 3.3 mg zinc powder (50.0 μmol, 20 mol%), 16.0 mg zinc iodide (50.0 μmol, 20 mol%), 0.1 mL of the 0.125 mM $HPPh_2$ solution (12.5 μmol, 5.0 mol%) and 64 mg (*Z*)-tetradeca-9,13-dien-1-yl acetate (0.25 mmol, 1.0 eq). The reaction mixture was stirred for 8 h at −15 °C. After general workup (9*Z*,12*Z*)-Tetradeca-9,12-dien-1-yl acetate was obtained as an *E*/*Z* mixture (12:88) in 92% yield (59 mg, 0.23 mmol) as colorless oil. The product mixture contained 4% of unreacted starting material. Pure 2-(*Z*)-configured product (**165**) was obtained after flash chromatography on silica gel impregnated with 10 weight-% $AgNO_3$ eluting with a stepwise gradient of *n*-pentane/EtOAc (40:1→10:1) as colorless oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 5.52 – 5.30 (m, 4H, C*H*$_{olef}$), 4.05 (t, *J* = 6.7 Hz, 2H, C*H*$_2$), 2.78 (t, *J* = 6.2 Hz, 2H, C*H*$_2$), 2.09 – 1.98 (m, 2H, C*H*$_2$), 2.04 (s, 3H, C*H*$_{3,\ Ac}$), 1.64 (ddd, *J* = 6.5, 2.5, 1.0 Hz, 3H, C*H*$_3$), 1.63 – 1.57 (m, 2H, C*H*$_2$), 1.31 (br s, 10H, C*H*$_2$).

^{13}C NMR (125 MHz, $CDCl_3$) δ 171.3 (*C*=O), 130.3 (*C*H_{olef}), 129.1 (*C*H_{olef}), 128.0 (*C*H_{olef}), 124.1 (*C*H_{olef}), 64.8 (*C*H_2), 29.8 (*C*H_2), 29.5 (*C*H_2), 29.4 (*C*H_2), 29.3 (*C*H_2), 28.8 (*C*H_2), 27.4 (*C*H_2), 26.1 (*C*H_2), 25.5 (*C*H_2), 21.1 (*C*$H_{3,\ Ac}$), 12.9 (*C*H_3).

IR (neat) 3014, 2926, 2855, 1741, 1656, 1458, 1387, 1365, 1234, 1125, 1100, 1039, 967, 893, 847, 722, 695, 634, 606, 421.

HRMS (EI) calculated for $C_{16}H_{28}O_2$: *m*/*z* = 252.2089; found *m*/*z* = 252.2097.

<u>Resolved signals of the minor product (9*Z*,12*E*)-tetradeca-9,12-dien-1-yl acetate:</u>

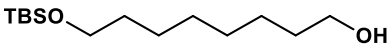
^{1}H NMR (300 MHz, $CDCl_3$) δ 5.48 – 5.31 (m, 4H, C*H*$_{olef}$), 4.05 (t, *J* = 6.8 Hz, 2H, C*H*$_2$), 2.72 (t, *J* = 5.0 Hz, 2H, C*H*$_2$), 2.06 – 1.95 (m, 2H, C*H*$_2$), 2.04 (s, 3H, C*H*$_{3,\ Ac}$), 1.66 – 1.56 (m, 5H, C*H*$_2$ + C*H*$_3$), 1.30 (br s, 10H, C*H*$_2$).

^{13}C NMR (75 MHz, $CDCl_3$) δ 171.3 (*C*=O), 130.5 (*C*H$_{olef}$), 129.8 (*C*H$_{olef}$), 127.9 (*C*H$_{olef}$), 125.2 (*C*H$_{olef}$), 64.8 (*C*H$_2$), 30.6 (*C*H$_2$), 29.8 (*C*H$_2$), 29.5 (*C*H$_2$), 29.4 (*C*H$_2$), 29.3 (*C*H$_2$), 28.8 (*C*H$_2$), 27.2 (*C*H$_2$), 26.1 (*C*H$_2$), 21.1 (*C*H$_{3,\ Ac}$), 18.0 (*C*H$_3$).

The NMR spectroscopic data for the minor product are in accordance with the literature.[117]

5.3.3 Synthesis of the Pheromone (8Z,10E)-Dodeca-8,10-dien-1-yl Acetate

8-((*tert*-Butyldimethylsilyl)oxy)octan-1-ol (285)



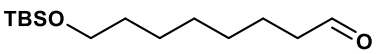
According to a procedure of Blair,[134] 1.50 g sodium hydride (60% dispersion in mineral oil, 37.5 mmol, 1.1 eq) were suspended in 250 mL anhydrous THF under argon atmosphere and 5.00 g 1,8-octanediol (34.2 mmol, 1.0 eq) were added at ambient temperature in one portion. The mixture was stirred overnight. Then, 5.20 g TBSCl (34.5 mmol, 1.0 eq) were added in one portion at 0 °C. Stirring was continued for another 4 h. After addition of water the mixture was extracted with EtOAc. The combined organic layers were washed with brine, dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure. The crude product was purified by FC (*n*-pentane/EtOAc 6:1) to give 8-((*tert*-butyldimethylsilyl)oxy)octan-1-ol (**285**) in 68% yield (6.04 g, 22.2 mmol) as colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ 3.66 – 3.57 (m, 4H, C*H*$_2$), 1.59 – 1.46 (m, 4H, C*H*$_2$), 1.31 (br s, 8H, C*H*$_2$), 0.89 (s, 9H, C(C*H*$_3$)$_3$), 0.04 (s, 6H, SiC*H*$_3$).

^{13}C NMR (75 MHz, $CDCl_3$) δ 63.4 (*C*H$_2$), 63.2 (*C*H$_2$), 33.02 (*C*H$_2$), 32.97 (*C*H$_2$), 29.6 (*C*H$_2$), 26.1 (C(*C*H$_3$)$_3$), 25.9 (*C*H$_2$), 25.8 (*C*H$_2$), 18.5 (*C*(CH$_3$)$_3$), –5.1 (Si*C*H$_3$).

The NMR spectroscopic data are in accordance with the literature.[136]

8-((*tert*-Butyldimethylsilyl)oxy)octanal (286)



According to a procedure of Sammis,[136] under argon atmosphere, 6.6 mL dimethyl sulfoxide (92.7 mmol, 4.0 eq) were added to a solution of 3.97 mL oxalyl chloride (46.4 mmol, 2.0 eq) in anhydrous CH_2Cl_2 (50 mL) at −78 °C dropwise over a period of 30 min. Then a solution of 6.038 g 8-((*tert*-butyldimethylsilyl)oxy)octan-1-ol (22.2 mmol, 1.0 eq) in 50 mL anhydrous CH_2Cl_2 was added over the same period of time and the mixture was stirred for another 90 min. Then, 25.7 mL triethylamine (185 mmol, 8.0 eq) were added dropwise and the resulting slurry was stirred overnight at ambient temperature. The mixture was poured into water and extracted with CH_2Cl_2, washed with water and brine, dried

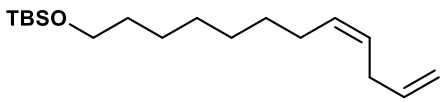
over $MgSO_4$, filtered and the solvent was removed by rotary evaporation. The crude product was purified by FC (*n*-pentane/Et_2O 5:1) to give 8-((*tert*-butyldimethylsilyl)oxy)octanal (**286**) in 87% yield (5.20 g, 20.1 mmol) as colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ 9.76 (t, *J* = 1.9 Hz, 1H, C*H*O), 3.59 (t, *J* = 6.5 Hz, 2H, CH_2), 2.41 (dt, *J* = 7.4, 1.9 Hz, 2H, CH_2), 1.32 (br s, 6H, CH_2), 0.89 (s, 9H, C(CH_3)$_3$), 0.04 (s, 6H, SiCH_3).

^{13}C NMR (75 MHz, $CDCl_3$) δ 202.9 (*C*=O), 63.3 (*C*H_2), 32.9 (*C*H_2), 29.3 (*C*H_2), 26.1 (C(*C*H_3)$_3$), 25.8 (*C*H_2), 22.2 (*C*H_2), 18.5 (*C*(CH$_3$)$_3$), –5.1 (Si*C*H_3).

The NMR spectroscopic data are in accordance with the literature.[136]

(*Z*)-*tert*-Butyl(dodeca-8,11-dien-1-yloxy)dimethylsilane (287)



According to a procedure of Hansson,[138] 5.95 g but-3-enyltriphenylphosphonium bromide (8.83 mmol, 1.0 eq) in 16 mL anhydrous THF were cooled to 0 °C and 3.5 mL *n*-BuLi (2.5 M in *n*-hexane, 8.83 mmol, 1.0 eq) were added *via* syringe. The suspension was stirred for 90 min at ambient temperature. It was then cooled to –60 °C and 3.06 mL anhydrous DMPU (23.8 mmol, 2.7 eq) were added. After 15 min 2.28 g 8-((*tert*-butyldimethylsilyl)oxy)octanal (8.83 mmol, 1.0 eq) were added and the mixture was stirred overnight at ambient temperature. NH_4Cl solution was added and the solution was extracted with Et_2O, dried over $MgSO_4$, filtered and the solvent was evaporated. The crude product was purified by FC (*n*-pentane/Et_2O 100:1) to give (*Z*)-*tert*-butyl(dodeca-8,11-dien-1-yloxy)dimethylsilane (**287**) in 62% (1.63 g, 5.48 mmol) as colorless oil.

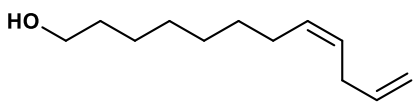
^{1}H NMR (500 MHz, $CDCl_3$) δ 5.85 – 5.77 (m, 1H, CH_{olef}), 5.48 – 5.35 (m, 2H, CH_{olef}), 5.03 (dq, *J* = 17.1, 1.8 Hz, 1H, CH_{olef}), 4.97 (dq, *J* = 10.1, 1.9 Hz, 1H, CH_{olef}), 3.60 (t, *J* = 6.5 Hz, 2H, CH_2), 2.79 (dt, *J* = 7.1, 1.6 Hz, 2H, CH_2), 2.03 (q, *J* = 7.0 Hz, 2H, CH_2), 1.52 – 1.48 (m, 2H, CH_2), 1.36 – 1.30 (m, 8H, CH_2), 0.90 (s, 9H, C(CH_3)$_3$), 0.05 (s, 6H, SiCH_3).

^{13}C NMR (125 MHz, $CDCl_3$) δ 137.3 (*C*H$_{olef}$), 131.3 (*C*H$_{olef}$), 126.8 (*C*H$_{olef}$), 114.6 (*C*H$_{2,\ olef}$), 63.5 (*C*H_2), 33.1 (*C*H_2), 31.7 (*C*H_2), 29.7 (*C*H_2), 29.5 (*C*H_2), 29.4 (*C*H_2), 27.3 (*C*H_2), 26.2 (C(*C*H_3)$_3$), 25.9 (*C*H_2), 18.5 (*C*(CH$_3$)$_3$), –5.1 (Si*C*H_3).

IR (neat) 3011, 2928, 2856, 1638, 1471, 1462, 1387, 1361, 1254, 1097, 1005, 992, 938, 910, 832, 813, 773, 712, 679, 661, 572, 541, 503.

HRMS (ESI) calculated for $C_{20}H_{40}OSi+H^+$: *m*/*z* = 325.2921; found *m*/*z* = 325.2930.

(*Z*)-Dodeca-8,11-dien-1-ol (288)



According to a procedure of Kalesse,[139] under argon atmosphere, 1.4 mL of a TBAF solution (1.0 M in THF, 5.47 mmol, 1.2 eq) were added to a solution of 1.35 g (*Z*)-*tert*-butyl(dodeca-8,11-dien-1-yloxy)dimethylsilane (4.56 mmol, 1.0 eq) in 40 mL anhydrous THF at 0 °C. After 1 h the reaction was quenched with water and extracted with Et_2O. The combined organic layers were washed with brine, dried over $MgSO_4$, filtered and concentrated by rotary evaporation. The crude product was purified by FC (*n*-pentane/MTBE 5:1) to give alcohol (*Z*)-dodeca-8,11-dien-1-ol (**288**) in 86% yield (717 mg, 3.93 mmol) as yellow oil.

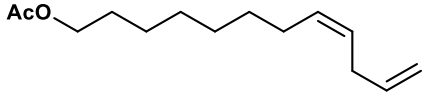
^{1}H NMR (300 MHz, $CDCl_3$) δ 5.88 – 5.74 (m, 1H, C*H*$_{olef}$), 5.49 – 5.34 (m, 2H, C*H*$_{olef}$), 5.03 (dq, *J* = 17.2, 1.8 Hz, 1H, C*H*$_{olef}$), 4.96 (dq, *J* = 10.1, 1.9 Hz, 1H, C*H*$_{olef}$), 3.64 (t, *J* = 6.6 Hz, 2H, C*H*$_2$), 2.79 (t, *J* = 6.3 Hz, 2H, C*H*$_2$), 2.03 (q, *J* = 7.0 Hz, 2H, C*H*$_2$), 1.61 – 1.52 (m, 2H, C*H*$_2$), 1.32 (br s, 8H, C*H*$_2$).

^{13}C NMR (75 MHz, $CDCl_3$) δ 137.3 (*C*H$_{olef}$), 131.2 (*C*H$_{olef}$), 126.8 (*C*H$_{olef}$), 114.7 (*C*H$_{2,\ olef}$), 63.2 (*C*H$_2$), 32.9 (*C*H$_2$), 31.7 (*C*H$_2$), 29.7 (*C*H$_2$), 29.4 (*C*H$_2$), 29.3 (*C*H$_2$), 27.3 (*C*H$_2$), 25.9 (*C*H$_2$).

IR (neat) 3323, 3079, 3009, 2926, 2854, 1637, 1462, 1432, 1376, 1272, 1056, 992, 909, 836, 775, 723, 635, 530.

HRMS (ESI) calculated for $C_{12}H_{22}O$: *m*/*z* = 182.1671; found *m*/*z* = 182.1655.

(*Z*)-Dodeca-8,11-dien-1-yl Acetate (194)



According to a procedure of Jamison,[140] 1.37 mL triethylamine (9.87 mmol, 3.0 eq), 504 mg acetic anhydride (4.94 mmol, 1.5 eq) and 40 mg DMAP (0.33 mmol, 10 mol%) were added to a solution of 600 mg (*Z*)-dodeca-8,11-dien-1-ol (3.29 mmol, 1.0 eq) in 7.0 mL anhydrous CH_2Cl_2 at 0 °C. The mixture was stirred for 5 h at ambient temperature, then quenched with NH_4Cl solution and extracted with Et_2O. The combined organic layers were washed with aqueous $NaHCO_3$, NH_4Cl, water and brine, dried over $MgSO_4$, filtered and the solvent was evaporated. The crude product was purified by FC (*n*-pentane/Et_2O 15:1) to give (*Z*)-dodeca-8,11-dien-1-yl acetate (**194**) in 90% yield (666 mg, 2.97 mmol) as colorless oil.

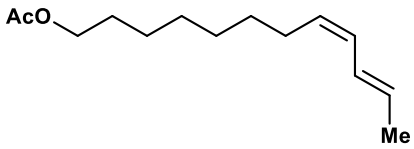
^{1}H NMR (500 MHz, $CDCl_3$) δ 5.88 – 5.80 (m, 1H, C*H*$_{olef}$), 5.51 – 5.39 (m, 2H, C*H*$_{olef}$), 5.06 (dq, *J* = 17.5, 2.0 Hz, 1H, C*H*$_{olef}$), 5.00 (dq, *J* = 10.1, 1.9 Hz, 1H, C*H*$_{olef}$), 4.08 (t, *J* = 6.6 Hz, 2H, C*H*$_2$), 2.83 – 2.81 (m, 2H, C*H*$_2$), 2.07 (s, 3H, C*H*$_{3,\ Ac}$), 2.03 (t, *J* = 7.1 Hz, 2H, C*H*$_2$), 1.67 – 1.62 (m, 2H, C*H*$_2$), 1.35 (br s, 8H, C*H*$_2$).

^{13}C NMR (125 MHz, $CDCl_3$) δ 171.3 (*C*=O), 137.3 (*C*H$_{olef}$), 131.2 (*C*H$_{olef}$), 126.9 (*C*H$_{olef}$), 114.7 (*C*H$_{2,\ olef}$), 64.7 (*C*H$_2$), 31.7 (*C*H$_2$), 29.6 (*C*H$_2$), 29.3 (*C*H$_{3,\ Ac}$), 28.8 (*C*H$_2$), 27.2 (*C*H$_2$), 26.1 (*C*H$_2$), 21.0 (*C*H$_2$).

IR (neat) 3080, 3009, 2928, 2856, 1739, 1638, 1464, 1435, 1388, 1365, 1232, 1036, 993, 910, 838, 723, 634, 605, 526.

HRMS (EI) calculated for $C_{14}H_{24}O_2$: *m*/*z* = 224.1776; found *m*/*z* = 224.1779.

(8*Z*,10*E*)-Dodeca-8,10-dien-1-yl Acetate (164)



The title compound was prepared according to GP 1 utilizing 32 mg Co(dppp)Br_2 (50.0 μmol, 10 mol%), 6.6 mg zinc powder (100 μmol, 20 mol%), 32.0 mg zinc iodide (100 μmol, 20 mol%), 0.2 mL of the 0.125 mM $HPPh_2$ solution (25.0 μmol, 5.0 mol%) and 112 mg (*Z*)-dodeca-8,11-dien-1-yl acetate (0.25 mmol, 1.0 eq). The reaction mixture was stirred for 16 h at ambient temperature. After general workup (8*Z*,10*E*)-dodeca-8,10-dien-1-yl acetate (**164**) was obtained as an *E*/*Z* mixture (87:13) in 90% yield (100 mg, 0.45 mmol) as colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ 6.06 – 5.90 (m, 2H, C*H*$_{olef}$), 5.62 – 5.48 (m, 2H, C*H*$_{olef}$), 4.04 (dt, *J* = 6.7, 1.2 Hz, 2H, C*H*$_2$), 2.04 (s, 3H, C*H*$_{3,\ Ac}$), 1.72 (d, *J* = 6.8 Hz, 3H, C*H*$_3$), 1.63 – 1.58 (m, 2H, C*H*$_2$), 1.30 (br s, 10H, C*H*$_2$).

^{13}C NMR (75 MHz, $CDCl_3$) δ 171.3 (*C*=O), 132.1 (*C*H$_{olef}$), 131.9 (*C*H$_{olef}$), 130.5 (*C*H$_{olef}$), 126.9 (*C*H$_{olef}$), 64.8 (*C*H$_2$), 32.6 (*C*H$_2$), 29.5 (*C*H$_2$), 29.3 (*C*H$_2$), 29.2 (*C*H$_2$), 28.8 (*C*H$_2$), 26.0 (*C*H$_2$), 21.1 (*C*H$_{3,\ Ac}$), 18.1 (*C*H$_3$).

Resolved signals of the minor product (8*Z*,10*Z*)-dodeca-8,10-dien-1-yl acetate:

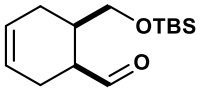
^{1}H NMR (300 MHz, $CDCl_3$) δ 6.36 – 6.24 (m, 2H, C*H*$_{olef}$), 5.70 – 5.65 (m, 2H, C*H*$_{olef}$), 1.76 (d, *J* = 6.8 Hz, 3H, C*H*$_3$).

^{13}C NMR (125 MHz, $CDCl_3$) δ 134.5 (*C*H$_{olef}$), 128.7 (*C*H$_{olef}$), 125.6 (*C*H$_{olef}$), 33.0 (*C*H$_2$), 29.8 (*C*H$_2$), 27.8 (*C*H$_2$), 18.4 (*C*H$_{3,\ Ac}$), 13.4 (*C*H$_3$).

The NMR spectroscopic data for the minor product are in accordance with the literature.[141]

5.3.4 Attempted Synthesis of Aucanthen

(*cis*)-6-(((*tert*-Butyldimethylsilyl)oxy)methyl)cyclohex-3-ene-1-carbaldehyde (199)



Under argon atmosphere, 2.8 mL oxalyl chloride (32.8 mmol, 2.0 eq) were dissolved in 50 mL anhydrous dichloromethane and cooled to −78 °C. 4.7 mL DMSO (65.6 mmol, 4.0 eq) in 50 mL anhydrous dichloromethane were added over a period of 30 min. After stirring for another 30 min at −78 °C 4.21 g ((*cis*)-6-(((*tert*-butyldimethylsilyl)oxy)methyl)cyclohex-3-en-1-yl)methanol (16.4 mmol, 1.0 eq) were added within 30 min at −78 °C. After 90 min 17.5 mL triethylamin (131 mmol, 8.0 eq) were added at −78 °C within 30 min and the reaction mixture was allowed to warm up to ambient temperature overnight. H_2O was added, and the aqueous layer was extracted three times with dichloromethane. The combined organic layers were washed with brine, dried over $MgSO_4$, filtered and the solvent was evaporated. The crude product was purified by FC (*n*-pentane/Et_2O 11:1) to give (*cis*)-6-(((*tert*-butyldimethylsilyl)oxy)methyl)cyclohex-3-ene-1-carbaldehyde (**199**) in 84% yield (3.49 g, 13.7 mmol) as colorless oil.

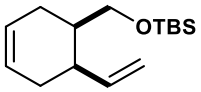
^{1}H NMR (300 MHz, $CDCl_3$) δ 9.74 (s, 1H, *H*CO), 5.73 – 5.60 (m, 2H, C*H*$_{olef}$), 3.63 – 3.52 (m, 2H, C*H*$_2$), 2.60 – 1.92 (m, 6H, C*H* + C*H*$_2$), 0.86 (s, 9H, C(C*H*$_3$)$_3$), 0.01 (d, *J* = 2.9 Hz, 6H, SiC*H*$_3$).

^{13}C NMR (75 MHz, $CDCl_3$) δ 203.9 (*C*=O), 125.9 (*C*H$_{olef}$), 125.1 (*C*H$_{olef}$), 63.6 (*C*H$_2$), 47.7 (*C*H), 36.6 (*C*H), 27.0 (*C*H$_2$), 26.0 (C(*C*H$_3$)$_3$) 22.1 (*C*H$_2$), 18.4 (Si*C*(CH$_3$)$_3$), −5.45 (Si*C*H$_3$).

IR (neat) 3027, 2953, 2928, 2898, 2856, 1721, 1471, 1389, 1251, 1093, 1077, 1006, 832, 774, 663, 401.

HRMS (EI) calculated for $C_{14}H_{26}O_2Si$: *m*/*z* = 254.1702; found *m*/*z* = 254.1700.

***tert*-Butyldimethyl(((*cis*)-6-vinylcyclohex-3-en-1-yl)methoxy)silane (289)**



Under argon atmosphere, 7.90 g methyltriphenylphosphonium bromide (22.1 mmol, 1.2 eq) and 2.80 g potassium *tert*-butoxide (25.0 mmol, 1.4 eq) were suspended in 60 mL anhydrous Et_2O and stirred for 20 min at ambient temperature. 4.86 g (*cis*)-6-(((*tert*-butyldimethylsilyl)oxy)methyl)cyclohex-3-ene-1-carbaldehyde (19.3 mmol, 1.0 eq) were added and the reaction mixture was stirred overnight at ambient temperature. NH_4Cl solution was added and the aqueous layer was extracted three times with Et_2O. The

combined organic layers were washed with brine, dried over $MgSO_4$, filtered and the solvent was evaporated. The crude product was purified by FC (*n*-pentane/Et_2O 50:1) to give *tert*-butyldimethyl(((*cis*)-6-vinylcyclohex-3-en-1-yl)methoxy)silane (**289**) in 72% yield (4.04 g, 16.0 mmol) as colorless oil.

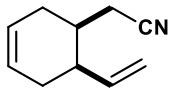
^{1}H NMR (300 MHz, $CDCl_3$) δ 5.67 – 5.59 (m, 3H, C*H*$_{olef}$), 5.05 – 4.95 (m, 2H, C*H*$_{2, olef}$), 3.61 – 3.40 (m, 2H, C*H*$_2$), 2.43 – 1.72 (m, 6H, C*H* + C*H*$_2$), 0.87 (s, 9H, C(C*H*$_3$)$_3$), 0.05 (s, 6H, SiC*H*$_3$).

^{13}C NMR (75 MHz, $CDCl_3$) δ 139.3 (*C*H$_{olef}$), 126.1 (*C*H$_{olef}$), 125.6 (*C*H$_{olef}$), 115.1 (*C*H$_{2, olef}$), 64.5 (*C*H$_2$), 37.9 (*C*H), 30.4 (*C*H$_2$), 26.1 (C(*C*H$_3$)$_3$), 25.8 (C*H*), 18.5 (Si*C*(CH$_3$)$_3$), –5.45 (Si*C*H$_3$).

IR (neat) 3075, 3024, 2954, 2927, 2896, 2856, 1637, 1471, 1253, 1079, 1000, 938, 833, 773, 655, 403.

HRMS (EI) calculated for $C_{14}H_{25}OSi$: *m*/*z* = 237.1675; found *m*/*z* = 237.1684.

(*cis*)-2-(6-Vinylcyclohex-3-en-1-yl)acetonitrile (290)



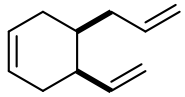
The title compound was prepared after quantitative deprotection of of *tert*-butyldimethyl(((*cis*)-6-vinylcyclohex-3-en-1-yl)methoxy)silane and mesylation of the corresponding alcohol. Then, 3.10 g ((*cis*)-6-vinylcyclohex-3-en-1-yl)methyl methanesulfonate (14.3 mmol, 1.0 eq) and 2.04 g 18-crown-6 (7.72 mmol, 54 mol%) were dissolved in 60 mL anhydrous acetonitrile followed by the addition of 1.86 g potassium cyanide (28.6 mmol, 2.0 eq) and 150 mg sodium iodide (1.00 mmol, 7.0 mol%). The reaction mixture was stirred for 60 h at 80 °C. H_2O was then added and the aqueous layer was extracted three times with MTBE. The combined organic layers were dried over $MgSO_4$, filtered and the solvent was evaporated. The crude product was purified by FC (*n*-pentane/Et_2O 8:1) to give (*cis*)-2-(6-vinylcyclohex-3-en-1-yl)acetonitrile (**290**) in 78% yield (1.64 g, 11.2 mmol) as colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ 5.83 – 5.52 (m, 3H, C*H*$_{olef}$), 5.22 – 5.08 (m, 2H, C*H*$_{2, olef}$), 2.81 – 1.82 (m, 8H, C*H* + C*H*$_2$).

^{13}C NMR (75 MHz, $CDCl_3$) δ 137.5 (*C*H$_{olef}$), 125.5 (*C*H$_{olef}$), 124.7 (*C*H$_{olef}$), 117.0 (*C*H$_{2, olef}$), 116.8 (*C*N), 39.8 (*C*H$_2$CN), 34.2 (*C*H), 30.3 (*C*H$_2$), 28.5 (*C*H$_2$) 25.8 (*C*H).

The NMR spectroscopic data are in accordance with the literature.[142]

(*cis*)-4-Allyl-5-vinylcyclohex-1-ene (200)



Under argon atmosphere, 1.64 g (*cis*)-2-(6-vinylcyclohex-3-en-1-yl)acetonitrile (11.2 mmol, 1.0 eq) were dissolved in 40 mL anhydrous THF and 23.5 mL DIBAL (1.0 M in THF, 23.5 mmol, 2.1 eq) were added at −78 °C. The reaction was stirred for 30 min at −78 °C and another 3 h at ambient temperature. Aqueous $NaHCO_3$ solution was added carefully and the aqueous layer was extracted three times with Et_2O. The combined organic layers were washed with brine, dried over $MgSO_4$, filtered and the solvent was evaporated. A preformed mixture of 5.59 g methyltriphenylphosphonium bromide (15.7 mmol, 1.4 eq) and 6.3 mL *n*-BuLi (2.5 M in *n*-hexane, 15.7 mmol, 1.4 eq) in 60 mL anhydrous THF was stirred for 2 h before crude (*cis*)-2-(6-vinylcyclohex-3-en-1-yl)acetaldehyde was added at 0 °C. The reaction mixture was stirred overnight at ambient temperature. The mixture was adsorbed on silica, the solvent was evaporated followed by purification by FC (*n*-pentane) to give (*cis*)-4-allyl-5-vinylcyclohex-1-ene (**200**) in 35% yield (583 mg, 3.93 mmol) as colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ 5.71-5.92 (m, 2H, C*H*$_{olef}$), 5.64 (s, 2H, C*H*$_{olef}$), 4.96-5.18 (m, 4H, C*H*$_{2,\ olef}$), 2.49 – 2.42 (m, 1H, C*H*), 2.34 – 1.74 (m, 7H, C*H* + C*H*$_2$).

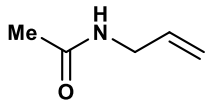
^{13}C NMR (75 MHz, $CDCl_3$) δ 139.5 (*C*H$_{olef}$), 137.9 (*C*H$_{olef}$), 126.3 (*C*H$_{olef}$), 125.5 (*C*H$_{olef}$), 115.7 (*C*H$_{2,\ olef}$), 115.2 (*C*H$_{2,\ olef}$), 40.4 (*C*H), 36.6 (*C*H$_2$), 36.5 (*C*H$_2$), 30.3 (*C*H), 28.7 (*C*H$_2$).

The NMR spectroscopic data are in accordance with the literature.[142]

5.4 Isomerization of *N*-Allyl Amides

5.4.1 Synthesis of N-Allyl Amides and Carbamates

_N_-Allylacetamide (71a)



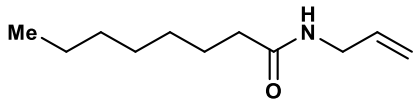
The title compound was prepared according to GP 2. First, 1.50 mL allylamine (20.0 mmol, 1.0 eq) and 4.16 mL triethylamine (30.0 mmol, 1.5 eq) were dissolved in 50 mL dichloromethane and 1.56 mL acetyl chloride (22.0 mmol, 1.1 eq) were added at 0 °C. After stirring overnight at ambient temperature, the reaction mixture was quenched with 0.1 M aqueous HCl and the aqueous layer was extracted three times with Et_2O. The combined organic layers were washed with brine, dried over Na_2SO_4, filtered and the solvent was evaporated. *N*-Allylacetamide (**71a**) was obtained in 43% yield (843 mg, 8.50 mmol) as colorless volatile liquid without further purification.

^{1}H NMR (300 MHz, $CDCl_3$) δ 5.83 (tdd, *J* = 16.6 Hz, 11.6 Hz, 5.9 Hz, 1H, C*H*$_{olef}$), 5.58 (s, 1H, N*H*), 5.21 – 5.11 (m, 2H, C*H*$_{2,\ olef}$), 3.87 (t, *J* = 5.4 Hz, 2H, C*H*$_2$), 2.00 (s, 3H, C*H*$_3$).

^{13}C NMR (75 MHz, $CDCl_3$) δ 170.0 (*C*=O), 134.4 (*C*H$_{olef}$), 116.6 (*C*H$_{2,\ olef}$), 42.2 (*C*H$_2$), 23.4 (*C*H$_3$).

The NMR spectroscopic data are in accordance with the literature.[143]

_N_-Allyloctanamide (71b)



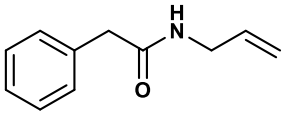
The title compound was prepared according to GP 2. First, 2.25 mL allylamine (30.0 mmol, 1.0 eq) and 4.16 mL triethylamine (30.0 mmol, 1.0 eq) were dissolved in 30 mL dichloromethane and 5.13 mL octanoyl chloride (30.0 mmol, 1.0 eq) were added at 0 °C. After stirring overnight at ambient temperature, the reaction mixture was quenched with H_2O and the aqueous layer was extracted three times with dichloromethane. The combined organic layers were washed with brine, dried over $MgSO_4$, filtered and the solvent was evaporated. The crude product was purified by FC (*n*-pentane/Et_2O 9:1) to give *N*-allyloctanamide (**71b**) in 87% yield (4.77 g, 26.0 mmol) as white solid.

^{1}H NMR (300 MHz, $CDCl_3$) δ 5.99 – 5.77 (m, 1H, C*H*$_{olef}$), 5.52 (s, 1H, N*H*), 5.20 – 5.10 (m, 2H, C*H*$_{2,\ olef}$) 3.88 (tt, *J* = 5.7, 1.5 Hz, 2H, C*H*$_2$), 2.19 (t, *J* = 7.3 Hz, 2H, C*H*$_2$), 1.63 (m, *J* = 7.3 Hz, 2H, C*H*$_2$), 1.28 (m, *J* = 3.6 Hz, 8H, C*H*$_2$), 0.87 (t, *J* = 6.9 Hz, 3H, C*H*$_3$).

^{13}C NMR (75 MHz, $CDCl_3$) δ 173.2 (*C*=O), 134.6 (*C*H_{olef}), 116.3 (*C*$H_{2,\ olef}$), 42.0 (*C*H_2), 36.9 (*C*H_2), 31.8 (*C*H_2), 29.4 (*C*H_2), 29.1 (*C*H_2), 25.9 (*C*H_2), 22.7 (*C*H_2), 14.1 (*C*H_3).

The NMR spectroscopic data are in accordance with the literature.[122]

N-Allyl-2-phenylacetamide (71c)



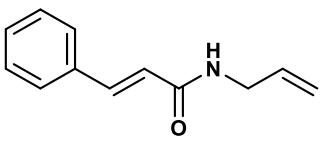
The title compound was prepared according to GP 2. First, 1.13 mL allylamine (15.0 mmol, 1.0 eq) and 2.06 mL triethylamine (15.0 mmol, 1.0 eq) were dissolved in 30 mL dichloromethane and 2.00 mL phenylacetyl chloride (15.0 mmol, 1.0 eq) were added at 0 °C. After stirring overnight at ambient temperature, the reaction mixture was quenched with H_2O and the aqueous layer was extracted three times with dichloromethane. The combined organic layers were washed with brine, dried over $MgSO_4$, filtered and the solvent was evaporated. Pure *N*-allyl-2-phenylacetamide (**71c**) was obtained in 94% yield (2.47 g, 14.1 mmol) as white solid without further purification.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.40 – 7. 26 (m, 5H, C*H*$_{ar}$), 5.83 – 5.70 (m, 1H, C*H*$_{olef}$), 5.42 (s, 1H, N*H*), 5.08 (d, *J* = 1.5 Hz, 1H, C*H*$_{olef}$), 5.03 (dd, *J* = 7.8, 1.5 Hz, 1H, C*H*$_{olef}$), 3.85 (tt, *J* = 5.6,1.5 Hz, 2H, C*H*$_2$), 3.61 (s, 2H, C*H*$_2$).

^{13}C NMR (75 MHz, $CDCl_3$) δ 170.9 (*C*=O), 135.0 (*C*$_{q,\ ar}$), 134.2 (*C*H_{olef}), 129.6 (*C*H_{ar}), 129.2 (*C*H_{ar}), 127.5 (*C*H_{ar}), 116.2 (*C*$H_{2,\ olef}$), 44.0 (*C*H_2), 42.0 (*C*H_2).

The NMR spectroscopic data are in accordance with the literature.[122]

N-Allylcinnamamide (71d)



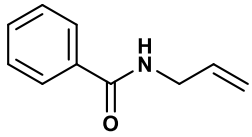
The title compound was prepared according to GP 2. First, 2.25 mL allylamine (30.0 mmol, 1.0 eq) and 4.16 mL triethylamine (30.0 mmol, 1.0 eq) were dissolved in 30 mL dichloromethane and 5.00 g cinnamoyl chloride (30.0 mmol, 1.0 eq) were added at 0 °C. After stirring overnight at ambient temperature, the reaction mixture was quenched with H_2O and the aqueous layer was extracted three times with dichloromethane. The combined organic layers were washed with brine, dried over $MgSO_4$, filtered and the solvent was evaporated. The crude product was purified by FC (*n*-pentane/Et_2O 3:1) to give *N*-allylcinnamamide (**71d**) in 59% yield (3.32 g, 17.8 mmol) as white solid.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.66 (d, *J* = 15.7 Hz, 1H, C*H*$_{olef}$), 7.52 – 7.49 (m, 2H, C*H*$_{ar}$), 7.39 – 7.35 (m, 3H, C*H*$_{ar}$), 6.41 (d, *J* = 15.5 Hz, 1H, C*H*$_{olef}$), 5.97 – 5.84 (m, 1H, C*H*$_{olef}$), 5.66 (s, 1H, N*H*), 5.24 (dd, *J* = 17.1, 1.4 Hz, 1H, C*H*$_{olef}$), 5.19 (dd, *J* = 10.2, 1.2 Hz, 1H, C*H*$_{olef}$), 4.03 (tt, *J* = 5.7, 1.5 Hz, 2H, C*H*$_2$).

^{13}C NMR (75 MHz, $CDCl_3$) δ 165.8 (*C*=O), 141,5 (*C*H$_{olef}$), 135.0 (*C*$_{q, ar}$), 134.3 (*C*H$_{olef}$), 129.9 (*C*H$_{ar}$), 129.0 (*C*H$_{ar}$), 128.0 (*C*H$_{ar}$), 120.6 (*C*H$_{olef}$), 116.8 (*C*H$_{2, olef}$), 42.3 (*C*H$_2$).

The NMR spectroscopic data are in accordance with the literature.[144]

***N*-Allylbenzamide (71e)**



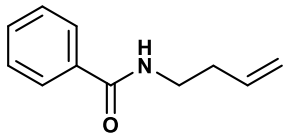
The title compound was prepared according to GP 2. First, 2.25 mL allylamine (30.0 mmol, 1.0 eq) and 4.16 mL triethylamine (30.0 mmol, 1.0 eq) were dissolved in 30 mL dichloromethane and 4.36 mL benzoyl chloride (37.5 mmol, 1.3 eq) were added at 0 °C. After stirring overnight at ambient temperature, the reaction mixture was quenched with H_2O and the aqueous layer was extracted three times with dichloromethane. The combined organic layers were washed with brine, dried over $MgSO_4$, filtered and the solvent was evaporated. The crude product was purified by FC (*n*-pentane/Et_2O 4:1) to give *N*-allylbenzamide (**71e**) in 89% yield (4.28 g, 26.6 mmol) as colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.78 (dd, *J* = 8.6, 1.4 Hz, 2H, C*H*$_{ar}$), 7.52 – 7.40 (m, 3H, C*H*$_{ar}$), 6.27 (s, 1H, N*H*), 6.00 – 5.88 (m, 1H, C*H*$_{olef}$), 5.25 (dd, *J* = 17.1, 1.4 Hz, 1H, C*H*$_{olef}$), 5.18 (dd, *J* = 10.2, 1.3 Hz, 1H, C*H*$_{olef}$), 4.09 (t, *J* = 5.7 Hz, 2H, C*H*$_2$).

^{13}C NMR (75 MHz, $CDCl_3$) δ 167.5 (*C*=O), 134.7 (*C*$_{q, ar}$), 134.3 (*C*H$_{olef}$), 131.6 (*C*H$_{ar}$), 128.7 (*C*H$_{ar}$), 127.1 (*C*H$_{ar}$), 116.8 (*C*H$_{2, olef}$), 42.6 (*C*H$_2$).

The NMR spectroscopic data are in accordance with the literature.[122]

***N*-(But-3-en-1-yl)benzamide (290)**



The title compound was prepared according to GP 2. First, 1.14 g but-3-enylamine (16.0 mmol, 1.0 eq) and 2.22 mL triethylamine (16.0 mmol, 1.0 eq) were dissolved in 16 mL dichloromethane and 1.84 mL benzoyl chloride (16.0 mmol, 1.0 eq) were added at 0 °C. After stirring overnight at ambient temperature, the reaction mixture was quenched with H_2O and the aqueous layer was extracted three times with dichloromethane. The combined organic layers were washed with

brine, dried over Na_2SO_4, filtered and the solvent was evaporated. The crude product was purified by FC (*n*-pentane/Et_2O 4:1) to give *N*-(but-3-en-1-yl)benzamide (**290**) in 25% yield (711 mg, 4.06 mmol) as colorless oil.

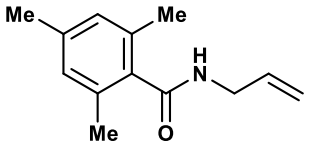
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.74 (t, *J* = 8.4, 1.5 Hz, 2H, C*H*$_{ar}$), 7.50 – 7.388 (m, 3H, C*H*$_{ar}$), 6.28 (s, 1H, N*H*), 5.83 (tdd, *J* = 17.2 Hz, 10.3 Hz, 7.0 Hz, 1H, C*H*$_{olef}$), 5.18 – 5.10 (m, 2H, C*H*$_{2, olef}$), 3.68 (q, *J* = 6.3 Hz, 2H, C*H*$_2$), 2.38 (q, *J* = 6.8 Hz, 2H, C*H*$_2$).

^{13}C NMR (75 MHz, $CDCl_3$) δ 167.6 (*C*=O), 135.5 (*C*H$_{olef}$), 134.9 (*C*$_{q, ar}$), 131.5 (*C*H$_{ar}$), 128.7 (*C*H$_{ar}$), 127.0 (*C*H$_{ar}$), 117.5 (*C*H$_{2, olef}$), 39.0 (*C*H$_2$), 33.9 (*C*H$_2$).

IR (neat) 3312, 3076, 2978, 2932, 1636, 1537, 1219, 1182, 915, 692.

HRMS (ESI) calculated for $C_{11}H_{13}NONa^+$: *m*/*z* = 198.0889; found *m*/*z* = 198.0891.

N-Allyl-2,4,6-trimethylbenzamide (71f)



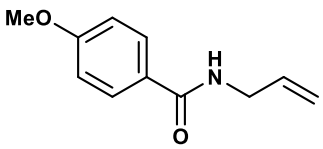
The title compound was prepared according to GP 2. First, 2.25 mL allylamine (30.0 mmol, 1.0 eq) and 4.16 mL triethylamine (30.0 mmol, 1.0 eq) were dissolved in 30 mL dichloromethane and 5.00 mL trimethylbenzoyl chloride (30.0 mmol, 1.0 eq) were added at 0 °C. After stirring overnight at ambient temperature, the reaction mixture was quenched with H_2O and the aqueous layer was extracted three times with dichloromethane. The combined organic layers were washed with brine, dried over $MgSO_4$, filtered and the solvent was evaporated. Pure *N*-allyl-2,4,6-trimethylbenzamide (**71f**) was obtained in 91% yield (5.53 g, 27.2 mmol) as white solid.

^{1}H NMR (300 MHz, $CDCl_3$) δ 6.84 (s, 2H, C*H*$_{ar}$), 6.00 – 5.87 (m, 1H, C*H*$_{olef}$), 5.67 (s, 1H, N*H*), 5.25 (dq, *J* = 17.2, 1.4 Hz, 1H, C*H*$_{olef}$), 5.20 (dd, *J* = 10.1, 1.5 Hz, 1H, C*H*$_{olef}$), 4.09 (tt, *J* = 5.8, 1.4 Hz, 2H, C*H*$_2$), 2.29 (s, 6H, C*H*$_{3, ortho}$), 2.27 (s, 3H, C*H*$_{3, para}$).

^{13}C NMR (75 MHz, $CDCl_3$) δ 170.5 (*C*=O), 138.6 (*C*$_{q, ar}$), 135.0 (*C*$_{q, ar}$), 134.3 (*C*$_{q, ar}$), 134.2 (*C*H$_{olef}$), 128.4 (*C*H$_{ar}$), 117.0 (*C*H$_{2, olef}$), 42.1 (*C*H$_2$), 21.2 (*C*H$_{3, para}$), 19.3 (*C*H$_{3, ortho}$).

The NMR spectroscopic data are in accordance with the literature.[122]

N-Allyl-4-methoxybenzamide (71g)



The title compound was prepared according to GP 2. First, 2.25 mL allylamine (30.0 mmol, 1.0 eq) and 4.16 mL triethylamine (30.0 mmol, 1.0 eq) were dissolved in 30 mL dichloromethane and

5.12 g 4-methoxybenzoyl chloride (30.0 mmol, 1.0 eq) were added at 0 °C. After stirring overnight at ambient temperature, the reaction mixture was quenched with H_2O and the aqueous layer was extracted three times with dichloromethane. The combined organic layers were washed with brine, dried over $MgSO_4$, filtered and the solvent was evaporated. The crude product was purified by FC (*n*-pentane/Et_2O 4:1) to give *N*-allyl-4-methoxybenzamide (**71g**) in 87% yield (4.97 g, 26.0 mmol) as pale redish solid (m.p. 45–52 °C).

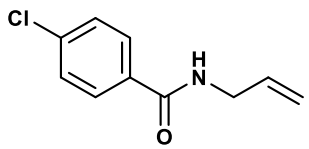
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.76 (d, *J* = 8.6 Hz, 2H, C*H*$_{ar}$), 6.92 (d, *J* = 8.8 Hz, 2H, C*H*$_{ar}$), 6.20 (s, 1H, N*H*), 6.00 – 5.87 (m, 1H, C*H*$_{olef}$), 5.23 (d, *J* = 17.2 Hz, 1H, C*H*$_{olef}$), 5.19 (dd, *J* = 10.2, 1.0 Hz, 1H, C*H*$_{olef}$), 4.07 (dt, *J* = 5.8, 0.9 Hz, 2H, C*H*$_2$), 3.84 (s, 3H, O-C*H*$_3$).

^{13}C NMR (75 MHz, $CDCl_3$) δ 167.0 (*C*=O), 162.3 (*C*$_{q, ar}$), 134.5 (*C*H$_{olef}$), 128.9 (*C*H$_{ar}$), 126.9 (*C*$_{q, ar}$), 116.6 (*C*H$_{2, olef}$), 113.9 (*C*H$_{ar}$), 55.5 (O-*C*H$_3$), 42.5 (*C*H$_2$).

IR (neat) 3328, 1606, 1542, 1504, 1297, 1250, 1178, 1026, 995, 920, 841, 765, 595.

HRMS (ESI) calculated for $C_{11}H_{13}NO_2Na^+$: *m*/*z* = 214.0838; found *m*/*z* = 214.0839.

***N*-Allyl-4-chlorobenzamide (71h)**



The title compound was prepared according to GP 2. First, 1.50 mL allylamine (20.0 mmol, 1.0 eq) and 2.77 mL triethylamine (20.0 mmol, 1.0 eq) were dissolved in 20 mL dichloromethane and 2.56 mL 4-chlorobenzoyl chloride (20.0 mmol, 1.0 eq) were added at 0 °C. After stirring overnight at ambient temperature, the reaction mixture was quenched with H_2O and the aqueous layer was extracted three times with dichloromethane. The combined organic layers were washed with brine, dried over $MgSO_4$, filtered and the solvent was evaporated. Pure *N*-allyl-4-chlorobenzamide (**71h**) was obtained in 81% yield (3.18 g, 16.3 mmol) as white solid (m.p. 65–69 °C).

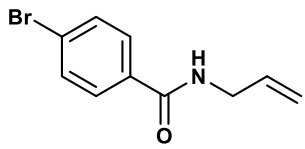
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.73 (d, *J* = 8.6 Hz, 2H, C*H*$_{ar}$), 7.41 (d, *J* = 8.6 Hz, 2H, C*H*$_{ar}$), 6.18 (s, 1H, N*H*), 6.00 – 5.87 (m, 1H, C*H*$_{olef}$), 5.24 – 5.18 (m, 2H, C*H*$_{2, olef}$), 4.08 (tt, *J* = 5.8, 1.5 Hz, 2H, C*H*$_2$).

^{13}C NMR (75 MHz, $CDCl_3$) δ 166.4 (*C*=O), 137.9 (*C*$_{q, ar}$), 134.1 (*C*H$_{olef}$), 133.0 (*C*$_{q, ar}$), 129.0 (*C*H$_{ar}$), 128.5 (*C*H$_{ar}$), 117.1 (*C*H$_{2, olef}$), 42.7 (*C*H$_2$).

IR (neat) 3280, 1631, 1592, 1533, 1483, 1273, 1153, 1088, 1013, 993, 930, 841, 758, 720, 648.

HRMS (ESI) calculated for $C_{10}H_{10}ClNONa^+$: *m*/*z* = 218.0343; found *m*/*z* = 218.0344.

N-Allyl-4-bromobenzamide (71i)



The title compound was prepared according to GP 2. First, 0.75 mL allylamine (10.0 mmol, 1.0 eq) and 1.78 mL triethylamine (10.0 mmol, 1.0 eq) were dissolved in 10 mL dichloromethane and 2.20 g 4-bromobenzoyl chloride (10.0 mmol, 1.0 eq) were added at 0 °C. After stirring overnight at ambient temperature, the reaction mixture was quenched with H_2O and the aqueous layer was extracted three times with dichloromethane. The combined organic layers were washed with brine, dried over $MgSO_4$, filtered and the solvent was evaporated. Pure *N*-allyl-4-bromobenzamide (**71i**) was obtained in 92% yield (2.12 g, 9.21 mmol) as white solid (m.p. 89–94 °C).

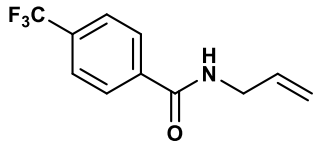
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.66 (d, *J* = 8.6 Hz, 2H, C*H*$_{ar}$), 7.57 (d, *J* = 8.6 Hz, 2H, C*H*$_{ar}$), 6.22 (s, 1H, N*H*), 5.99 – 5.86 (m, 1H, C*H*$_{olef}$), 5.25 (dd, *J* = 17.2, 1.4 Hz, 1H, C*H*$_{olef}$), 5.20 (dd, *J* = 15.9, 1.4 Hz, 1H, C*H*$_{olef}$), 4.07 (tt, *J* = 5.8, 1.4 Hz, 2H, C*H*$_2$).

^{13}C NMR (75 MHz, $CDCl_3$) δ 166.5 (*C*=O), 134.1 (*C*H$_{olef}$), 133.5 (*C*$_{q, ar}$), 132.0 (*C*H$_{ar}$), 128.7 (*C*H$_{ar}$), 126.3 (*C*$_{q, ar}$), 117.1 (*C*H$_{2, olef}$), 42.7 (*C*H$_2$).

IR (neat) 3289, 1628, 1587, 1530, 1457, 1347, 1274, 1148, 1066, 1008, 929, 842, 756, 702, 646, 620, 525, 449.

HRMS (ESI) calculated for $C_{10}H_{10}BrNONa^+$: *m*/*z* = 263.9818; found *m*/*z* = 263.9819.

N-Allyl-4-trifluoromethylbenzamide (71j)



The title compound was prepared according to GP 2. First, 0.60 mL allylamine (8.00 mmol, 1.0 eq) and 1.10 mL triethylamine (8.00 mmol, 1.0 eq) were dissolved in 8.0 mL dichloromethane and 1.67 g 4-trifluoromethylbenzoyl chloride (8.00 mmol, 1.0 eq) were added at 0 °C. After stirring overnight at ambient temperature, the reaction mixture was quenched with H_2O and the aqueous layer was extracted three times with dichloromethane. The combined organic layers were washed with brine, dried over $MgSO_4$, filtered and the solvent was evaporated. The crude product was purified by FC (*n*-pentane/EtOAc 8:1 → 3:1) to give *N*-allyl-4-trifluoromethylbenzamide (**71j**) in 95% yield (1.732 g, 7.56 mmol) as white solid (m.p. 102–105 °C).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.88 (d, *J* = 8.2 Hz, 2H, C*H*$_{ar}$), 7.67 (d, *J* = 8.2 Hz, 2H, C*H*$_{ar}$), 6.43 (s, 1H, N*H*), 5.99 – 5.86 (m, 1H, C*H*$_{olef}$), 5.25 (dd, *J* = 17.2, 1.2 Hz, 1H, C*H*$_{olef}$), 5.19 (dd, *J* = 10.2, 1.0 Hz, 1H, C*H*$_{olef}$), 4.09 (t, *J* = 5.7 Hz, 2H, C*H*$_2$).

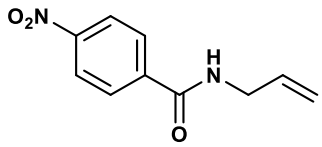
^{19}F NMR (283 MHz, $CDCl_3$) δ = –63.09 (s, C*F*$_3$).

^{13}C NMR (75 MHz, $CDCl_3$) δ 166.3 (*C*=O), 137.9 (*C*$_{q, ar}$), 133.9 (*C*H$_{olef}$), 133.4 (q, *J* = 32.7 Hz, CF_3*C*$_{q, ar}$), 127.6 (*C*H$_{ar}$), 125.7 (q, *J* = 3.8 Hz, *C*H$_{ar}$), 123.9 (q, *J* = 272.1 Hz, *C*F_3), 117.2 (*C*H$_{2, olef}$), 42.7 (*C*H_2).

IR (neat) 3294, 1651, 1638, 1577, 1542, 1508, 1423, 1407, 1362, 1326, 1308, 1266, 1152, 1121, 1081, 1066, 1031, 1017, 998, 982, 963, 919, 857, 843, 771, 697, 674, 626, 593, 558, 509, 474, 434.

HRMS (ESI) calculated for $C_{11}H_{10}F_3NONa^+$: *m*/*z* = 252.0607; found *m*/*z* = 252.0609.

***N*-Allyl-4-nitrobenzamide (205e)**



The title compound was prepared according to GP 2. First, 2.25 mL allylamine (30.0 mmol, 1.0 eq) and 4.16 mL triethylamine (30.0 mmol, 1.0 eq) were dissolved in 30 mL dichloromethane and 5.57 g 4-nitrobenzoyl chloride (30.0 mmol, 1.0 eq) were added at 0 °C. After stirring overnight at ambient temperature, the reaction mixture was quenched with H_2O and the aqueous layer was extracted three times with dichloromethane. The combined organic layers were washed with brine, dried over $MgSO_4$, filtered and the solvent was evaporated. The crude product was purified by FC (*n*-pentane/Et_2O 4:1) to give *N*-allyl-4-nitrobenzamide (**205e**) in 97% yield (5.99 g, 29.1 mmol) as white solid (m.p. 110–115°C).

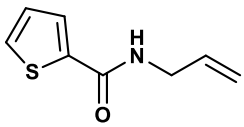
^{1}H NMR (300 MHz, $CDCl_3$) δ 8.26 (dd, *J* = 6.9, 1.9 Hz, 2H, C*H*$_{ar}$), 7.94 (dd, *J* = 6.9, 1.9 Hz, 2H, C*H*$_{ar}$), 6.49 (s, 1H, N*H*), 5.99 – 5.86 (m, 1H, C*H*$_{olef}$), 5.26 (dd, *J* = 17.2, 1.3 Hz, 1H, C*H*$_{olef}$), 5.20 (dd, *J* = 10.2, 1.2 Hz, 1H, C*H*$_{olef}$), 4.09 (ddt, *J* = 5.8, 1.3, 1.2 Hz, 2H, C*H*$_2$).

^{13}C NMR (75 MHz, $CDCl_3$) δ 165.5 (*C*=O), 149.8 (*C*$_{q, ar}$), 140.2 (*C*$_{q, ar}$), 133.6 (*C*H$_{olef}$), 128.3 (*C*H$_{ar}$), 123.9 (*C*H$_{ar}$), 117.5 (*C*H$_{2, olef}$), 42.9 (*C*H_2).

IR (neat) 3316, 3107, 2926, 1652, 1637, 1597, 1543, 1514, 1488, 1344, 1301, 1256, 930, 724, 706, 687.

HRMS (ESI) calculated for $C_{10}H_{10}N_2O_3Na^+$: *m*/*z* = 229.0584; found *m*/*z* = 229.0584.

_N_-Allylthiophene-2-carboxamide (71k)



The title compound was prepared according to GP 2. First, 1.50 mL allylamine (20.0 mmol, 1.0 eq) and 2.77 mL triethylamine (20.0 mmol, 1.0 eq) were dissolved in 20 mL dichloromethane and 2.17 mL thiophencarbonyl chloride (20.0 mmol, 1.0 eq) in 8 mL dichloromethane were added at 0 °C. After stirring overnight at ambient temperature, the reaction mixture was quenched with H_2O and the aqueous layer was extracted three times with dichloromethane. The combined organic layers were washed with brine, dried over Na_2SO_4, filtered and the solvent was evaporated. The crude product was adsorbed on silica and purified by FC (*n*-pentane/EtOAc 6:1) to give *N*-allylthiophene-2-carboxamide (**71k**) in 94% yield (3.19 g, 18.7 mmol) as white solid (m.p. 62–65°C).

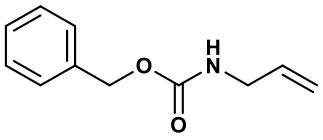
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.52 (d, *J* = 3.7 Hz, 1H, C*H*$_{ar}$), 7.47 (d, *J* = 4.9 Hz, 1H, C*H*$_{ar}$), 7.07 (t, *J* = 4.3 Hz, 1H, C*H*$_{ar}$), 6.09 (s, 1H, N*H*), 5.93 (tdd, *J* = 16.8 Hz, 11.5 Hz, 6.5 Hz, 1H, C*H*$_{olef}$), 5.26 (d, *J* = 17.6 Hz, 1H, C*H*$_{olef}$), 5.19 (d, *J* = 10.2 Hz, 1H, C*H*$_{olef}$), 4.06 (t, *J* = 5.6 Hz, 2H, C*H*$_2$).

^{13}C NMR (75 MHz, $CDCl_3$) δ 161.8 (*C*=O), 139.0 (*C*$_{q, ar}$), 134.2 (*C*H$_{olef}$), 130.0 (*C*H$_{ar}$), 128.2 (*C*H$_{ar}$), 127.7 (*C*H$_{ar}$), 117.0 (*C*H$_{2, olef}$), 42.5 (*C*H$_2$).

IR (neat) 3297, 3074, 1619, 1546, 1514, 1418, 1354, 1302, 1246, 1209, 1144, 1021, 960, 911, 856, 791, 751, 708, 664, 545.

HRMS (ESI) calculated for $C_8H_{10}NOS$: *m*/*z* = 168.0478; found *m*/*z* = 168.0478.

Benzyl-*N*-allylcarbamate (203b)



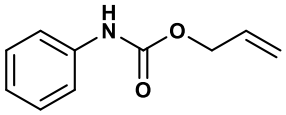
First, 2.25 mL allylamine (30.0 mmol, 1.0 eq) and 5.04 g $NaHCO_3$ (60.0 mmol, 2.0 eq) were suspended in 60 mL of a 1:1 EtOH/H_2O solvent mixture. 4.71 mL CbzCl (33.0 mmol, 1.1 eq) were added at 0 °C within 1 h and the reaction mixture was stirred overnight at ambient temperature. H_2O was then added, and the aqueous layer was extracted three times with MTBE. The combined organic layers were dried over $MgSO_4$, filtered and the solvent was evaporated. The crude product was purified by FC (*n*-pentane/MTBE 1:1) to give benzyl-*N*-allylcarbamate (**203b**) in 30% yield (1.73 g, 9.06 mmol) as colorless oil after additional evaporation of CbzCl in vacuo at 120 °C.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.37 – 7.28 (m, 5H, C*H*$_{ar}$), 5.91 – 5.79 (m, 1H, C*H*$_{olef}$), 5.19 (dq, *J* = 17.3, 1.4 Hz, 1H, C*H*$_{olef}$), 5.14 – 5.12 (m, 3H, C*H*$_{olef}$ + C*H*$_2$), 3.82 (t, *J* = 5.4 Hz, 2H, C*H*$_2$).

^{13}C NMR (75 MHz, $CDCl_3$) δ 156.4 (*C*=O), 136.7 ($C_{q,\,ar}$), 134.6 (CH_{olef}), 128.6 (CH_{ar}), 128.2 (CH_{ar}), 116.2 (CH_{olef}), 68.9 (CH_2), 43.7 (CH_2).

The NMR spectroscopic data are in accordance with the literature.[145]

Allyl-*N*-phenylcarbamate (203c)



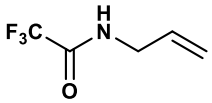
According to a procedure of Knowles,[146] 1.63 mL phenylisocyanate (15.0 mmol, 1.0 eq) and 1.02 mL allylalcohol (15.0 mmol, 1.0 eq) were dissolved in 30 mL anhydrous THF and 2.08 mL triethylamine (15.0 mmol, 1.0 eq) were added at 0 °C. After stirring for 90 min at ambient temperature the reaction mixture was quenched with H_2O and the aqueous layer was extracted three times with dichloromethane. The combined organic layers were washed with brine, dried over $MgSO_4$, filtered and the solvent was evaporated. The crude product was purified by recrystallization from *n*-hexane to give allyl-*N*-phenylcarbamate (**203c**) in 78% yield (2.07 g, 11.7 mmol) as yellowish solid.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.38 – 7.24 (m, 4H, C*H*$_{ar}$), 7.05 (t, *J* = 7.14 Hz, 1H, C*H*$_{ar}$), 6.66 (s, 1H, N*H*), 6.02 – 5.89 (m, 1H, C*H*$_{olef}$), 5.32 (d, *J* = 17.4 Hz, 1H, C*H*$_{olef}$), 5.28 (d, *J* = 10.5 Hz, 1H, C*H*$_{olef}$), 4.65 (d, *J* = 5.6 Hz, 2H, C*H*$_2$).

^{13}C NMR (75 MHz, $CDCl_3$) δ 153.4 (*C*=O), 137.9 ($C_{q,\,ar}$), 132.6 (CH_{olef}), 129.2 (CH_{ar}), 123.7 (CH_{ar}), 118.9 (CH_{ar}), 118.4 ($CH_{2,\,olef}$), 66.0 (CH_2).

The analytic data are in accordance with the literature.[146]

***N*-Allyl-2,2,2-trifluoroacetamide (205a)**



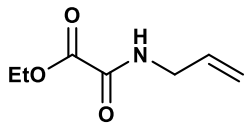
According to a procedure of Harned,[147] 0.77 mL trifluoroacetic acid (10.0 mmol, 1.0 eq) and 2.77 mL triethylamine (20.0 mmol, 2.0 eq) were dissolved in 33 mL anhydrous dichloromethane and 0.95 mL ethylchloroformiate (10.0 mmol, 1.0 eq) were added at 0 °C. After 30 min 0.90 mL allylamine (12.0 mmol, 1.2 eq) were added and the reaction mixture was stirred overnight. Aqueous $NaHCO_3$ solution was then added and the aqueous layer was extracted three times with dichloromethane. The combined organic layers were washed with brine, dried over Na_2SO_4, filtered and the solvent was evaporated. The crude product was adsorbed on silica and purified by FC (*n*-pentane/EtOAc 4:1) to give *N*-allyl-2,2,2-trifluoroacetamide (**205a**) in 35% yield (531 mg, 3.47 mmol) as colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ 6.36 (s, 1H, N*H*), 5.85 (tdd, *J* = 17.0 Hz, 11.3 Hz, 6.7 Hz, 1H, CH_{olef}), 5.30 – 5.24 (m, 2H, C$H_{2,\ olef}$), 3.99 (t, *J* = 6.0 Hz, 2H, CH_2).

^{13}C NMR (75 MHz, $CDCl_3$) δ 157.0 (*C*=O), 132.0 (*C*H_{olef}), 118.5 (*C*F_3, *C*$H_{2,\ olef}$), 42.3 (*C*H_2).

The NMR spectroscopic data are in accordance with the literature.[147]

Ethyl 2-(allylamino)-2-oxoacetate (205b)



Under argon atmosphere, 1.72 mL oxalyl chloride (20.0 mmol, 2.0 eq) was stirred at ambient temperature and 0.6 mL anhydrous EtOH (10.0 mmol, 1.0 eq) were added within 30 min. The reaction mixture was cooled to 0 °C and a mixture of 3.32 mL triethylamine (24.0 mmol, 2.4 eq) and 1.8 mL allylamine (24.0 mmol, 2.4 eq) were added. After stirring for 2 h at ambient temperature the reaction was quenched with H_2O and extracted three times with dichloromethane. The combined organic layers were dried over $MgSO_4$, filtered and the solvent was evaporated. The crude product was purified by FC (*n*-pentane/Et_2O 3:1) to give ethyl 2-(allylamino)-2-oxoacetate (**205b**) in 27% yield (837 mg, 5.33 mmol) as yellowish oil.

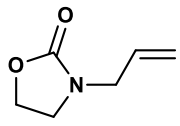
^{1}H NMR (300 MHz, $CDCl_3$) δ 5.91 – 5.78 (m, 1H, CH_{olef}), 5.27 – 5.18 (m, 2H, C$H_{2,\ olef}$), 4.34 (q, *J* = 7.1 Hz, 2H, CH_2), 3.96 (tt, *J* = 6.0, 1.4 Hz, 2H, CH_2), 1.38 (t, *J* = 7.2 Hz, 3H, CH_3).

^{13}C NMR (75 MHz, $CDCl_3$) δ 160.8 (*C*=O), 156.5 (*C*=O), 132.8 (*C*H_{olef}), 117.7 (*C*$H_{2,\ olef}$), 63.4 (*C*H_2), 42.3 (*C*H_2), 14.1 (*C*H_3).

IR (neat) 3297, 3082, 2986, 2939, 1734, 1683, 1646, 1524, 1467, 1421, 1393, 1370, 1339, 1302, 1258, 1201, 1097, 1016, 921, 860, 822, 806, 760, 733, 699, 955, 545.

HRMS (EI) calculated for $C_7H_{11}NO_3$: *m*/*z* = 157.0739; found *m*/*z* = 157.0734.

3-Allyloxazolidin-2-one (209b)



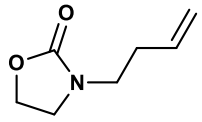
According to a procedure of Cushman,[148] 9.78 g cesium carbonate (30.0 mmol, 3.0 eq) were dissolved in 36 mL acetone. Then, 873 mg 2-oxazolidinone (10.0 mmol, 1.0 eq) and 1.1 mL allylbromide (13.0 mmol, 1.3 eq) were added. After stirring for 48 h at 60 °C the reaction mixture was filtered, and the solvent was evaporated. The crude product was adsorbed on silica and purified by FC (*n*-pentane/EtOAc 3:1) to give 3-allyloxazolidin-2-one (**209b**) in 97% yield (1.23 g, 9.67 mmol) as colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ 5.78 (tdd, *J* = 16.9 Hz, 10.8 Hz, 6.8 Hz, 1H, C*H*$_{olef}$), 5.27 – 5.22 (m, 2H, C*H*$_{2, olef}$), 4.33 (t, *J* = 7.9 Hz, 2H, C*H*$_2$), 3.87 (d, *J* = 6.2 Hz, 2H, C*H*$_2$), 3.52 (t, *J* = 8.5 Hz, 2H, C*H*$_2$).

^{13}C NMR (75 MHz, $CDCl_3$) δ 158.4 (*C*=O), 132.2 (*C*H$_{olef}$), 118.8 (*C*H$_{2, olef}$), 61.9 (*C*H$_2$), 47.2 (*C*H$_2$), 44.3 (*C*H$_2$).

The NMR spectroscopic data are in accordance with the literature.[149]

3-(But-3-en-1-yl)oxazolidin-2-one (217)



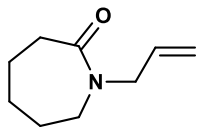
According to a procedure of Cushman,[148] 9.78 g cesium carbonate (30.0 mmol, 3.0 eq) were dissolved in 36 mL acetone. 873 mg 2-oxazolidinone (10.0 mmol, 1.0 eq) and 1.32 mL 4-bromobut-1-ene (13.0 mmol, 1.3 eq) were added. After stirring for 48 h at 60 °C the reaction mixture was filtered, and the solvent was evaporated. The crude product was adsorbed on silica and purified by FC (*n*-pentane/EtOAc 3:1) to give 3-(but-3-en-1-yl)oxazolidin-2-one (**217**) in 52% yield (732 mg, 5.18 mmol) as colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ 5.79 (tdd, *J* = 17.2 Hz, 10.3 Hz, 6.9 Hz, 1H, C*H*$_{olef}$), 5.16 – 5.06 (m, 2H, C*H*$_{2, olef}$), 4.31 (t, *J* = 7.9 Hz, 2H, C*H*$_2$), 3.57 (t, *J* = 8.0 Hz, 2H, C*H*$_2$), 3.35 (t, *J* = 7.1 Hz, 2H, C*H*$_2$), 2.33 (q, *J* = 7.0 Hz, 2H, C*H*$_2$).

^{13}C NMR (75 MHz, $CDCl_3$) δ 134.8 (*C*H$_{olef}$), 117.4 (*C*H$_{2, olef}$), 61.8 (*C*H$_2$), 44.8 (*C*H$_2$), 43.7 (*C*H$_2$), 32.1 (*C*H$_2$).

The NMR spectroscopic data are in accordance with the literature.[148]

1-Allylazepan-2-one (209c)



According to a procedure of Tokunaga,[149] 1.20 g NaH (60%, dispersion in mineral oil, 30.0 mmol, 1.5 eq) were suspended in 20 mL anhydrous THF. Then, 2.49 g caprolactame (20.0 mmol, 1.0 eq) were added at 0 °C. The reaction mixture was stirred overnight at 60 °C. 2.23 mL allylbromide (22.0 mmol, 1.1 eq) were added followed by further stirring at ambient temperature overnight. The reaction mixture was quenched with H_2O and the aqueous layer was extracted three times with Et_2O. The combined organic layers were dried over Na_2SO_4, filtered and the solvent was evaporated. The crude product was adsorbed on silica and purified by FC (*n*-pentane/EtOAc 4:1) to give 1-allylazepan-2-one (**209c**) in 85% yield (2.61 g, 17.0 mmol) as white solid.

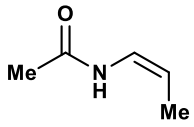
^{1}H NMR (300 MHz, $CDCl_3$) δ 5.76 (tdd, *J* = 16.8 Hz, 10.7 Hz, 6.0 Hz, 1H, C*H*$_{olef}$), 5.18 – 5.12 (m, 2H, C*H*$_{2,\ olef}$), 4.00 (d, *J* = 6.1 Hz, 2H, C*H*$_2$), 3.29 (t, *J* = 4.9 Hz, 2H, C*H*$_2$), 2.54 (t, *J* = 5.4 Hz, 2H, C*H*$_2$), 1.75 – 1.57 (m, 6H, C*H*$_2$).

^{13}C NMR (75 MHz, $CDCl_3$) δ 175.7 (*C*=O), 134.0 (*C*H$_{olef}$), 117.3 (*C*H$_{2,\ olef}$), 50.6 (*C*H$_2$), 48.8 (*C*H$_2$), 37.3 (*C*H$_2$), 30.1 (*C*H$_2$), 28.6 (*C*H$_2$), 23.6 (*C*H$_2$).

The NMR spectroscopic data are in accordance with the literature.[149]

5.4.2 Isomerization of N-Allyl Amides and Carbamates

(*Z*)-*N*-(Prop-1-en-1-yl)acetamide (72a)



The title compound was prepared according to GP 3 utilizing 28 mg Ni(dppp)Cl_2 (50.0 μmol, 10 mol%), 6.6 mg zinc powder and 32 mg zinc iodide (100 μmol, 20 mol% each). These materials were suspended in 0.3 mL dichloromethane and stirred for 10 min. Then, 0.2 mL of the $HPPh_2$ solution (0.125 M in dichloromethane, 25.0 μmol, 5.0 mol%) were added. After cooling to –20 °C, 50 mg *N*-allylacetamide (0.505 mmol, 1.0 eq) were added. The reaction mixture was stirred for 2 d at –20 °C. After general workup and purification by FC (*n*-pentane/EtOAc 1:1) *N*-(prop-1-en-1-yl)acetamide (**72a**) was obtained as *Z*/*E*-mixture (80:20) in 12% yield (6 mg, 0.061 mmol) as colorless, highly volatile liquid.

^{1}H NMR (300 MHz, $CDCl_3$) δ = 6.91 (s, 1H, N*H*), 6.74 – 6.68 (m, 1H, NC*H*$_{olef}$), 4.79 (dq, *J* = 8.3, 7.1 Hz, 1H, C*H*$_{olef}$), 2.08 (s, 3H, C*H*$_3$), 1.61 (dd, *J* = 7.0, 1.7 Hz, 3H, CH$_{olef}$C*H*$_3$).

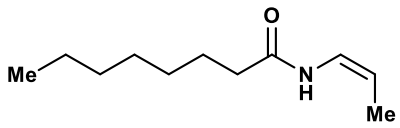
^{13}C NMR (125 MHz, $CDCl_3$) δ = 200.9 (*C*=O), 122.1 (N*C*H$_{olef}$), 104.9 (*C*H$_{olef}$), 23.5 (*C*H$_3$), 10.9 (CH$_{olef}$*C*H$_3$).

Resolved signals of the minor isomer (*E*)-*N*-(prop-1-en-1-yl)acetamide:

^{1}H NMR (300 MHz, $CDCl_3$) δ = 5.15 – 5.08 (m, 1H, C*H*$_{olef}$), 2.01 (s, 3H, C*H*$_3$), 1.66 (dd, *J* = 6.5, 1.5 Hz, 3H, CH$_{olef}$C*H*$_3$).

The NMR spectroscopic data for both isomers are in accordance with the literature.[43]

(*Z*)-*N*-(Prop-1-en-1-yl)octanamide (72b)



The title compound was prepared according to GP 3 utilizing 28 mg Ni(dppp)Cl_2 (50.0 μmol, 10 mol%), 6.6 mg zinc powder and 32 mg zinc iodide (100 μmol, 20 mol% each). These materials were suspended in 0.3 mL dichloromethane and stirred for 10 min. Then, 0.2 mL of the $HPPh_2$ solution (0.125 M in dichloromethane, 25.0 μmol, 5.0 mol%) were added. 92 mg *N*-allyloctanamide (0.502 mmol, 1.0 eq) were added at ambient temperature and the reaction mixture was stirred for 90 min. After general workup and purification by FC (*n*-pentane/Et_2O 7:1) *N*-(prop-1-en-1-yl)octanamide (**72b**) was obtained as *Z*/*E*-mixture (82:18) in 42% yield (39 mg, 0.213 mmol) as white solid (m.p. 32–35 °C).

^{1}H NMR (300 MHz, $CDCl_3$) δ = 6.86 (br s, 1H, N*H*), 6.74 (qq, *J* = 8.8, 1.6 Hz, 1H, NCH_{olef}), 4.78 (dq, *J* = 15.6, 7.7 Hz, 1H, CH_{olef}), 2.26 (t, *J* = 7.8 Hz, 2H, CH_2), 1.69 – 1.59 (m, 5H, CH_2 + $CH_{olef}CH_3$), 1.29 (dd, *J* = 7.1, 1.4 Hz, 8H, CH_2), 0.88 (t, *J* = 6.9 Hz, 3H, CH_3).

^{13}C NMR (75 MHz, $CDCl_3$) δ = 170.3 (*C*=O), 122.2 (NCH_{olef}), 104.7 (CH_{olef}), 37.0 (CH_2), 31.8 (CH_2), 29.4 (CH_2), 29.1 (CH_2), 25.7 (CH_2), 22.7 (CH_2), 14.2 (CH_3), 10.9 ($CH_{olef}CH_3$).

IR (neat) 3190, 2957, 2944, 2917, 2854, 1678, 1650, 1513, 1465, 1456, 1410, 1383, 1324, 1274, 1260, 1232, 1213, 1195, 1149, 1028, 952, 925, 740, 708, 599, 577.

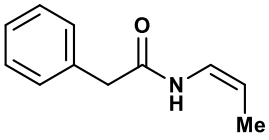
HRMS (ESI) *m*/*z* $[M+H]^+$ calculated for $C_{11}H_{22}NO$: 183.1696; found: 183.1696.

Resolved signals of the minor isomer (*E*)-*N*-(prop-1-en-1-yl)octanamide:

^{1}H NMR (300 MHz, $CDCl_3$) δ = 5.12 (dq, *J* = 14.0, 6.8 Hz, 1H, CH_{olef}), 2.18 (t, *J* = 7.9 Hz, 2H, CH_2), 1.68 – 1.64 (m, 3H, $CH_{olef}CH_3$).

^{13}C NMR (75 MHz, $CDCl_3$) δ = 123.5 (NCH_{olef}), 107.4 (CH_{olef}), 36.8 (CH_2), 14.9 (CH_3).

(*Z*)-2-Phenyl-*N*-(prop-1-en-1-yl)acetamide (72c)



The title compound was prepared according to GP 3 utilizing 28 mg Ni(dppp)Cl_2 (50.0 μmol, 10 mol%), 6.6 mg zinc powder and 32 mg zinc iodide (100 μmol, 20 mol% each). These materials were suspended in 0.3 mL dichloromethane and stirred for 10 min. Then, 0.2 mL of the $HPPh_2$ solution (0.125 M in dichloromethane, 25.0 μmol, 5.0 mol%) were added. After cooling to –30 °C, 88 mg *N*-allyl-2-phenylacetamide (0.502 mmol, 1.0 eq) were added. The reaction mixture was stirred for 64 h

at –30 °C. After general workup and purification by FC (*n*-pentane/Et_2O 2:1) 2-phenyl-*N*-(prop-1-en-1-yl)acetamide (**72c**) was obtained as *Z*/*E*-mixture (92:8) in 60% yield (53 mg, 0.303 mmol) as colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.42 – 7.28 (m, 5H, CH_{ar}), 6.86 (s, 1H, N*H*), 6.69 (tt, *J* = 9.7, 1.8 Hz, 1H, NCH_{olef}), 4.76 (dq, *J* = 15.6, 7.6 Hz, 1H, CH_{olef}), 3.66 (s, 2H, CH_2), 1.36 (dd, *J* = 7.0, 1.6 Hz, 3H, CH_3).

^{13}C NMR (75 MHz, $CDCl_3$) δ = 168.0 (*C*=O), 134.5 ($C_{q, ar}$), 129.6 (*C*H_{ar}), 129.4 (*C*H_{ar}), 127.8 (*C*H_{ar}), 121.9 (N*C*H_{olef}), 105.8 (*C*H_{olef}), 43.9 (*C*H_2), 10.6 (*C*H_3).

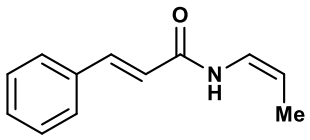
Resolved signals of the minor isomer (*E*)-2-phenyl-*N*-(prop-1-en-1-yl)acetamide:

^{1}H NMR (300 MHz, $CDCl_3$) δ = 5.01 (dq, *J* = 14.0, 6.8 Hz, 1H, CH_{olef}), 3.60 (s, 2H, CH_2), 1.61 (dd, *J* = 6.8, 1.5 Hz, 3H, CH_3).

^{13}C NMR (75 MHz, $CDCl_3$) δ = 14.8 (*C*H_3).

The NMR spectroscopic data for both isomers are in accordance with the literature.[50]

(*Z*)/(*E*)-*N*-(Prop-1-en-1-yl)cinnamamide (72d)



The title compound was prepared according to GP 3 utilizing 28 mg Ni(dppp)Cl_2 (50.0 μmol, 10 mol%), 6.6 mg zinc powder and 32 mg zinc iodide (100 μmol, 20 mol% each). These materials were suspended in 0.3 mL acetonitrile and stirred for 10 min. Then, 0.2 mL of the $HPPh_2$ solution (0.125 M in acetonitrile, 25.0 μmol, 5.0 mol%) were added. 94 mg *N*-allylcinnamamide (0.502 mmol, 1.0 eq) were added at ambient temperature and the reaction mixture was stirred for 6 d at 83 °C. After general workup and purification by FC (*n*-pentane/Et_2O 4:1) *N*-(prop-1-en-1-yl)cinnamamide (**72d**) was obtained as *Z*/*E*-mixture (50:50) in 54% yield (51 mg, 0.272 mmol) as white solid.

^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.73 (d, *J* = 15.5 Hz, 1H, PhCH_{olef}), 7.54 – 7.48 (m, 2H, CH_{ar}), 7.38 – 7.35 (m, 3H, CH_{ar}), 6.96 – 6.86 (m, 1H, NCH_{olef}), 6.47 (d, *J* = 15.5 Hz, 1H, CH_{olef}), 4.90 (dq, *J* = 15.8, 8.0 Hz, 1H, CH_{olef}), 1.70 (dt, *J* = 7.5, 1.5 Hz, 3H, CH_3).

^{13}C NMR (75 MHz, $CDCl_3$) δ = 163.0 (*C*=O), 142.2 (*C*H_{olef}), 134.8 ($C_{q, ar}$), 130.0 (*C*H_{ar}), 128.99 (*C*H_{ar}), 128.1 (*C*H_{ar}), 122.3 (*C*H_{olef}), 120.0 (N*C*H_{olef}), 106.1 (*C*H_{olef}), 11.2 (*C*H_3).

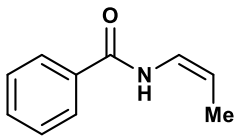
Resolved signals of (*E*)-*N*-(prop-1-en-1-yl)cinnamamide:

^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.70 (d, *J* = 15.5 Hz, 1H, PhC*H*$_{olef}$), 6.41 (d, *J* = 15.6 Hz, 1H, C*H*$_{olef}$), 5.26 (dq, *J* = 14.1, 6.9 Hz, 1H, C*H*$_{olef}$).

^{13}C NMR (75 MHz, $CDCl_3$) δ = 162.8 (*C*=O), 142.7 (*C*H$_{olef}$), 134.9 (*C*$_{q, ar}$), 130.1 (*C*H$_{ar}$), 128.96 (*C*H$_{ar}$), 128.0 (*C*H$_{ar}$), 123.7 (*C*H$_{olef}$), 120.2 (N*C*H$_{olef}$), 108.7 (*C*H$_{olef}$), 15.1 (*C*H$_3$).

The NMR spectroscopic data for both isomers are in accordance with the literature.[50]

(*Z*)-*N*-(Prop-1-en-1-yl)benzamide (72e)



The title compound was prepared according to GP 3 utilizing 28 mg Ni(dppp)Cl_2 (50.0 μmol, 10 mol%), 6.6 mg zinc powder and 32 mg zinc iodide (100 μmol, 20 mol% each). These materials were suspended in 0.3 mL dichloromethane and stirred for 10 min. Then, 0.2 mL of the $HPPh_2$ solution (0.125 M in dichloromethane, 25.0 μmol, 5.0 mol%) were added. After cooling to –30 °C, 83 mg *N*-allylbenzamide (0.514 mmol, 1.0 eq) were added. The reaction mixture was stirred for 64 h at –30 °C. After general workup and purification by FC (*n*-pentane/Et_2O 4:1) *N*-(prop-1-en-1-yl)benzamide (**72e**) was obtained as *Z*/*E*-mixture (91:9) in 74% yield (61 mg, 0.379 mmol) as white solid.

^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.80 (dd, *J* = 7.0, 1.5 Hz, 2H, C*H*$_{ar}$), 7.60 (s, 1H, N*H*), 7.56 – 7.43 (m, 3H, C*H*$_{ar}$), 6.94 (ddq, *J* = 10.7, 7.2, 1.7 Hz, 1H, NC*H*$_{olef}$), 4.94 (dq, *J* = 14.4, 7.3 Hz, 1H, C*H*$_{olef}$), 1.70 (dd, *J* = 7.1, 1.8 Hz, 3H, C*H*$_3$).

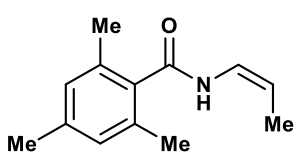
^{13}C NMR (75 MHz, $CDCl_3$) δ = 164.4 (*C*=O), 134.2 (*C*$_{q, ar}$), 132.0 (*C*H$_{ar}$), 128.9 (*C*H$_{ar}$), 127.2 (*C*H$_{ar}$), 122.4 (N*C*H$_{olef}$), 106.2 (*C*H$_{olef}$), 11.1 (*C*H$_3$).

Resolved signals of the minor isomer (*E*)-*N*-(prop-1-en-1-yl)benzamide:

^{1}H NMR (300 MHz, $CDCl_3$) δ = 5.32 (dq, *J* = 13.6, 6.9 Hz, 1H, C*H*$_{olef}$), 1.73 (dd, *J* = 6.7, 1.7 Hz, 3H, C*H*$_3$).

The NMR spectroscopic data for both isomers are in accordance with the literature.[50]

(*Z*)-2,4,6-Trimethyl-*N*-(prop-1-en-1-yl)benzamide (72f)



The title compound was prepared according to GP 3 utilizing 28 mg Ni(dppp)Cl_2 (50.0 μmol, 10 mol%), 6.6 mg zinc powder and 32 mg zinc iodide (100 μmol, 20 mol% each). These materials were

suspended in 0.3 mL dichloromethane and stirred for 10 min. Then, 0.2 mL of the $HPPh_2$ solution (0.125 M in dichloromethane, 25.0 μmol, 5.0 mol%) were added. 102 mg *N*-allyl-2,4,6-trimethylbenzamide (0.502 mmol, 1.0 eq) were added at ambient temperature and the reaction mixture was stirred for 7 d at ambient temperature. Additional 14 mg $Ni(dppp)Cl_2$ (25.0 μmol, 5.0 mol%), 3.3 mg zinc powder and 16 mg zinc iodide (50 μmol, 10 mol% each) and 0.1 mL of the $HPPh_2$ solution (0.125 M in dichloromethane, 12.5 μmol, 2.5.0 mol%) were added to the reaction mixture after 48 h as well as 4 d of stirring at ambient temperature to complete the conversion of the starting material. After general workup and purification by FC (*n*-pentane/Et_2O 4:1) 2,4,6-trimethyl-*N*-(prop-1-en-1-yl)benzamide (**72f**) was obtained as *Z*/*E*-mixture (86:14) in 47% yield (48 mg, 0.236 mmol) as white solid (m.p.123-128 °C). The *Z*-isomer appears as rotameric mixture.

^{1}H NMR (500 MHz, $CDCl_3$) δ (main rotamer) = 7.05 (d, *J* = 9.6 Hz, 1H, N*H*), 6.96 – 6.90 (m, 1H, NCH_{olef}), 6.88 (s, 2H, CH_{ar}), 4.91 (dq, *J* = 13.7, 7.4 Hz, 1H, CH_{olef}), 2.30 (s, 9H, $CH_{ar}CH_3$), 1.59 (dd, *J* = 7.3, 1.0 Hz, 3H, CH_3). δ (resolved signals minor rotamer) = 6.86 (s, 2H, CH_{ar}), 5.77 – 5.72 (m, 1H, CH_{olef}), 4.54 (dq, *J* = 14.8, 7.9 Hz, 1H, CH_{olef}), 2.22 (s, 9H, $C_{ar}CH_3$), 1.63 (dd, *J* = 7.4, 1.7 Hz, 3H, CH_3).

^{13}C NMR (125 MHz, $CDCl_3$) δ (main rotamer) = 167.7 (*C*=O), 139.1 ($C_{q, ar}$), 134.7 ($C_{q, ar}$), 128.5 ($C_{q, ar}$), 128.4 (CH_{ar}), 121.9 (NCH_{olef}), 106.1 (CH_{olef}), 21.2 ($C_{ar}CH_3$), 19.4 ($CH_{ar}CH_3$), 11.1 (CH_3). δ (resolved signals minor rotamer) = 167.6 (*C*=O), 138.95 ($C_{q, ar}$), 128.40 ($C_{q, ar}$), 123.6 (NCH_{olef}), 104.8 (CH_{olef}), 19.1 ($C_{ar}CH_3$), 10.6 (CH_3).

IR (neat) 3257, 3177, 2917, 2858, 1730, 1677, 1641, 1503, 1438, 1319, 1286, 1177, 1142, 1114, 1015, 965, 882, 749, 726, 622, 485, 449.

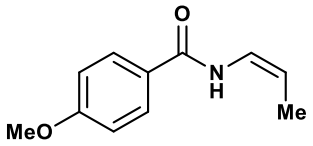
HRMS (ESI) *m*/*z* $[M+Na]^+$ calculated for $C_{13}H_{17}NONa$: 226.1202; found: 226.1204.

Resolved signals of the minor isomer (*E*)-2,4,6-trimethyl-*N*-(prop-1-en-1-yl)benzamide:

^{1}H NMR (300 MHz, $CDCl_3$) δ = 6.84 (s, 2H, CH_{ar}), 5.22 – 5.15 (m, 1H, CH_{olef}), 2.27 (s, 9H, $C_{ar}CH_3$), 1.72 (d, *J* = 6.9 Hz, 3H, CH_3).

^{13}C NMR (125 MHz, $CDCl_3$) δ = 171.4 (*C*=O), 138.92 ($C_{q, ar}$), 128.38 ($C_{q, ar}$), 123.4 (NCH_{olef}), 108.6 (CH_{olef}), 21.3 ($C_{ar}CH_3$), 19.3 ($C_{ar}CH_3$), 15.0 (CH_3).

(*Z*)-4-Methoxy-*N*-(Prop-1-en-1-yl)benzamide (72g)



The title compound was prepared according to GP 3 utilizing 28 mg Ni(dppp)Cl_2 (50.0 μmol, 10 mol%), 6.6 mg zinc powder and 32 mg zinc iodide (100 μmol, 20 mol% each). These materials were suspended in 0.3 mL dichloromethane and stirred for 10 min. Then, 0.2 mL of the $HPPh_2$ solution (0.125 M in dichloromethane, 25.0 μmol, 5.0 mol%) were added. 96 mg *N*-allyl-4-methoxybenzamid (0.502 mmol, 1.0 eq) were added at ambient temperature and the reaction mixture was stirred for 8 d at ambient temperature. After general workup and purification by FC (*n*-pentane/Et_2O 4:1→2:1) 4-methoxy-*N*-(Prop-1-en-1-yl)benzamide (**72g**) was obtained as *Z*/*E*-mixture (64:36) in 70% yield (67 mg, 0.350 mmol) as colorless oil which solidifies upon storage.

^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.77 (t, *J* = 7.4 Hz, 2H, CH_{ar}), 7.52 (s, 1H, N*H*), 6.94 (t, *J* = 8.4 Hz, 3H, CH_{ar} + NCH_{olef}), 4.90 (dq, *J* = 14.2, 7.1 Hz, 1H, CH_{olef}), 3.86 (s, 3H, OCH_3), 1.72 (t, *J* = 7.1 Hz, 3H, CH_3).

^{13}C NMR (75 MHz, $CDCl_3$) δ = 163.9 ($CH_3OC_{q,\ ar}$), 162.7 (*C*=O), 129.0 (*C*H_{ar}), 126.4 (N*C*H_{olef}), 122.6 ($C_{q,\ ar}$), 114.1 (*C*H_{ar}), 105.5 (*C*H_{olef}), 55.59 (O*C*H_3), 11.0 (*C*H_3).

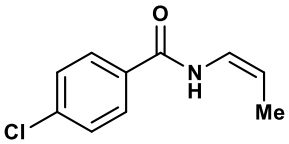
The NMR spectroscopic data are in accordance with the literature.[150]

Resolved signals of the minor isomer (*E*)-4-methoxy-*N*-(prop-1-en-1-yl)benzamide:

^{1}H NMR (300 MHz, $CDCl_3$) δ = 5.27 (dq, *J* = 14.2, 6.8 Hz, 1H, CH_{olef}), 3.85 (s, 3H, OCH_3), 1.71 (t, *J* = 6.9 Hz, 3H, CH_3).

^{13}C NMR (75 MHz, $CDCl_3$) δ = 162.6 (*C*=O), 128.9 (*C*H_{ar}), 126.3 (N*C*H_{olef}), 124.0 ($C_{q,\ ar}$), 114.0 (*C*H_{ar}), 108.2 (*C*H_{olef}), 55.56 (O*C*H_3), 15.1 (*C*H_3).

(*Z*)-4-Chloro-*N*-(prop-1-en-1-yl)benzamide (72h)



The title compound was prepared according to GP 3 utilizing 28 mg Ni(dppp)Cl_2 (50.0 μmol, 10 mol%), 6.6 mg zinc powder and 32 mg zinc iodide (100 μmol, 20 mol% each). These materials were suspended in 0.3 mL dichloromethane and stirred for 10 min. Then, 0.2 mL of the $HPPh_2$ solution (0.125 M in dichloromethane, 25.0 μmol, 5.0 mol%) were added. After cooling to –20 °C, 98 mg *N*-allyl-4-chlorobenzamide (0.501 mmol, 1.0 eq) were added. The reaction mixture was stirred for 39 h at –20 °C. After general workup and purification by FC

(*n*-pentane/Et_2O 4:1) 4-chloro-*N*-(prop-1-en-1-yl)benzamide (**72h**) was obtained as *Z*/*E*-mixture (81:19) in 66% yield (65 mg, 0.332 mmol) as white solid (m.p. 87-89 °C).

^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.74 (d, *J* = 8.5 Hz, 2H, C*H*$_{ar}$), 7.54 (s, 1H, N*H*), 7.44 (d, *J* = 8.7 Hz, 2H, C*H*$_{ar}$), 6.95 – 6.88 (m, 1H, NC*H*$_{olef}$), 4.97 (dq, *J* = 14.4, 7.1 Hz, 1H, C*H*$_{olef}$), 1.71 (dd, *J* = 7.1, 1.7 Hz, 3H, C*H*$_3$).

^{13}C NMR (75 MHz, $CDCl_3$) δ = 163.4 (*C*=O), 138.4 (*C*$_{q, ar}$), 132.5 (*C*$_{q, ar}$), 129.2 (*C*H$_{ar}$), 128.6 (*C*H$_{ar}$), 122.3 (N*C*H$_{olef}$), 106.7 (*C*H$_{olef}$), 11.1 (*C*H$_3$).

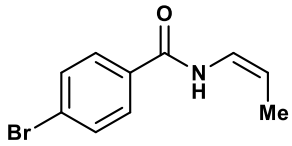
IR (neat) 3290, 1637, 1593, 1516, 1479, 1276, 1149, 1091, 1013, 953, 868, 843, 731, 666, 524, 489, 442.

HRMS (ESI) *m*/*z* $[M+Na]^+$ calculated for $C_{10}H_{10}ClNONa$: 218.0343; found: 218.0344.

<u>Resolved signals of the minor isomer (*E*)-4-chloro-*N*-(prop-1-en-1-yl)benzamide:</u>
^{1}H NMR (300 MHz, $CDCl_3$) δ = 5.32 (dq, *J* = 14.1, 6.7 Hz, 1H, C*H*$_{olef}$).

^{13}C NMR (75 MHz, $CDCl_3$) δ = 129.1 (*C*H$_{ar}$), 123.6 (N*C*H$_{olef}$), 109.4 (*C*H$_{olef}$), 15.1 (*C*H$_3$).

(*Z*)-4-Bromo-*N*-(prop-1-en-1-yl)benzamide (72i)



The title compound was prepared according to GP 3 utilizing 28 mg $Ni(dppp)Cl_2$ (50.0 μmol, 10 mol%), 6.6 mg zinc powder and 32 mg zinc iodide (100 μmol, 20 mol% each). These materials were suspended in 0.3 mL dichloromethane and stirred for 10 min. Then, 0.2 mL of the $HPPh_2$ solution (0.125 M in dichloromethane, 25.0 μmol, 5.0 mol%) were added. After cooling to –25 °C, 120 mg *N*-allyl-4-bromobenzamide (0.502 mmol, 1.0 eq) were added. The reaction mixture was stirred for 69 h at –25 °C. After general workup and purification by FC (*n*-pentane/Et_2O 4:1) 4-bromo-*N*-(prop-1-en-1-yl)benzamide (**72i**) was obtained as *Z*/*E*-mixture (93:7) in 62% yield (74 mg, 0.310 mmol) as white solid. The isomers are separable through FC (m.p. 94-98 °C for the *Z*-isomer, 160 °C for the *E*-isomer).

^{1}H NMR (300 MHz, $CDCl_3$) δ = δ 7.67 (d, *J* = 8.6 Hz, 2H, C*H*$_{ar}$), 7.58 (d, *J* = 8.6 Hz, 2H, C*H*$_{ar}$), 6.89 (dt, *J* = 9.8, 1.6 Hz, 1H, NC*H*$_{olef}$), 4.96 (dq, *J* = 15.9, 7.8 Hz, 1H, C*H*$_{olef}$), 1.70 (dd, *J* = 7.1, 1.6 Hz, 3H, C*H*$_3$).

^{13}C NMR (75 MHz, $CDCl_3$) δ = 163.5 (*C*=O), 133.0 (*C*$_{q, ar}$), 132.2 (*C*H$_{ar}$), 128.8 (*C*H$_{ar}$), 126.8 (N*C*H$_{olef}$), 122.3 (*C*$_{q, ar}$), 106.8 (*C*H$_{olef}$), 11.1 (*C*H$_3$).

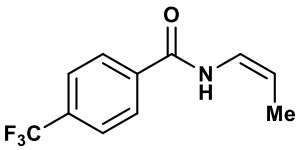
IR (neat) 3295, 1636, 1589, 1509, 1477, 1366, 1273, 1178, 1147, 1068, 1008, 866, 837, 728, 673, 611, 512, 446.

HRMS (ESI) *m/z* $[M+Na]^+$ calculated for $C_{10}H_{10}BrNONa$: 263.9818; found: 263.9821.

Resolved signals of the minor isomer (*E*)-4-bromo-*N*-(prop-1-en-1-yl)benzamide:

^{1}H NMR (300 MHz, $CDCl_3$) δ = 5.26 (dq, *J* = 14.0, 6.9 Hz, 1H, C*H*$_{olef}$).

(*Z*)-*N*-(Prop-1-en-1-yl)-4-(trifluoromethyl)benzamide (72j)



The title compound was prepared according to GP 3 utilizing 28 mg $Ni(dppp)Cl_2$ (50.0 μmol, 10 mol%), 6.6 mg zinc powder and 32 mg zinc iodide (100 μmol, 20 mol% each). These materials were suspended in 0.3 mL dichloromethane and stirred for 10 min. Then, 0.2 mL of the $HPPh_2$ solution (0.125 M in dichloromethane, 25.0 μmol, 5.0 mol%) were added. After cooling to 18 °C, 113 mg *N*-allyl-4-trifluoromethylbenzamide (0.493 mmol, 1.0 eq) were added. The reaction mixture was stirred for 45 h at 18 °C. After general workup and purification by FC (*n*-pentane/Et_2O 4:1) *N*-(prop-1-en-1-yl)-4-(trifluoromethyl)benzamide (**72j**) was obtained as *Z*/*E*-mixture (78:22) in 63% yield (71 mg, 0.310 mmol) as white solid (m.p. 172 °C).

^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.92 (d, *J* = 8.0 Hz, 2H, C*H*$_{ar}$), 7.73 (d, *J* = 8.4 Hz, 2H, C*H*$_{ar}$), 7.59 (br s, 1H, N*H*), 6.99 – 6.89 (m, 1H, NC*H*$_{olef}$), 5.00 (dq, *J* = 14.5, 7.1 Hz, 1H, C*H*$_{olef}$), 1.72 (dd, *J* = 7.0, 1.8 Hz, 3H, C*H*$_3$).

^{13}C NMR (125 MHz, $CDCl_3$) δ = 163.3 (*C*=O), 133.7 (q, *J* = 32.9 Hz, $CF_3C_{q,\,ar}$), 127.7 (*C*H$_{ar}$), 125.9 (q, *J* = 3.7 Hz, *C*H$_{ar}$), 123.7 (q, *J* = 272.6 Hz, *C*F$_3$), 122.1 (NC*H*$_{olef}$), 107.4 (C*H*$_{olef}$), 11.2 (C*H*$_3$).

^{19}F NMR (283 MHz, $CDCl_3$) δ = –63.13 (s, C*F*$_3$).

IR (neat) 3294, 1678, 1635, 1580, 1529, 1505, 1438, 1409, 1320, 1258, 1162, 1119, 1076, 1062, 1016, 954, 859, 847, 795, 726, 693, 680, 600, 469.

HRMS (ESI) *m/z* $[M+H]^+$ calculated for $C_{11}H_{11}F_3NO$: 230.0787; found: 230.0789.

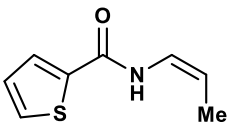
Resolved signals of the minor isomer (*E*)-*N*-(prop-1-en-1-yl)-4-(trifluoromethyl)benzamide:

^{1}H NMR (300 MHz, $CDCl_3$) δ = 5.36 (dq, *J* = 14.8, 7.3 Hz, 1H, C*H*$_{olef}$), 1.75 (dd, *J* = 7.0, 1.6 Hz, 3H, C*H*$_3$).

^{13}C NMR (125 MHz, $CDCl_3$) δ = 163.0 (*C*=O), 137.3 ($C_{q, ar}$), 125.8 (q, *J* = 3.9 Hz, *C*H$_{ar}$), 123.4 (N*C*H$_{olef}$), 110.1 (*C*H$_{olef}$), 15.1 (*C*H$_3$).

^{19}F NMR (283 MHz, $CDCl_3$) δ = –63.12 (s, 3F, C*F*$_3$).

(*Z*)-*N*-(Prop-1-en-1-yl)thiophene-2-carboxamide (72k)



The title compound was prepared according to GP 3 utilizing 28 mg Ni(dppp)Cl_2 (50.0 μmol, 10 mol%), 6.6 mg zinc powder and 32 mg zinc iodide (100 μmol, 20 mol% each). These materials were suspended in 0.3 mL dichloromethane and stirred for 10 min. Then, 0.2 mL of the $HPPh_2$ solution (0.125 M in dichloromethane, 25.0 μmol, 5.0 mol%) were added. After cooling to 5 °C, 84 mg *N*-allylthiophene-2-carboxamide (0.502 mmol, 1.0 eq) were added. The reaction mixture was stirred for 3 d at 5 °C. After general workup and purification by FC (*n*-pentane/Et_2O 4:1) *N*-(prop-1-en-1-yl)thiophene-2-carboxamide (**72k**) was obtained as *Z*/*E*-mixture (84:16) in 33% yield (28 mg, 0.167 mmol) as colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ = δ 7.57 (dd, *J* = 3.6, 0.9 Hz, 1H, C*H*$_{ar}$), 7.52 (dd, *J* = 5.1, 0.9 Hz, 1H, C*H*$_{ar}$), 7.43 (s, 1H, N*H*), 7.11 (dd, *J* = 4.9, 1.1 Hz, 1H, C*H*$_{ar}$), 6.91 – 6.84 (m, 1H, NC*H*$_{olef}$), 4.92 (dq, *J* = 8.5, 7.3 Hz, 1H, C*H*$_{olef}$), 1.70 (dd, *J* = 7.1, 1.7 Hz, 3H, C*H*$_3$).

^{13}C NMR (75 MHz, $CDCl_3$) δ = 158.9 (*C*=O), 138.4 ($C_{q, ar}$), 130.8 (*C*H$_{ar}$), 128.7 (*C*H$_{ar}$), 127.9 (*C*H$_{ar}$), 122.0 (N*C*H$_{olef}$), 106.1 (*C*H$_{olef}$), 11.1 (*C*H$_3$).

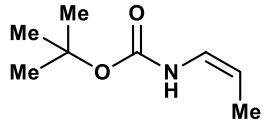
Resolved signals of the minor isomer (*E*)-*N*-(prop-1-en-1-yl)thiophene-2-carboxamide:

^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.08 (dd, *J* = 5.0, 1.0 Hz, 1H, C*H*$_{ar}$), 5.29 (m, 1H, C*H*$_{olef}$).

^{13}C NMR (75 MHz, $CDCl_3$) δ = 130.6 (*C*H$_{ar}$), 128.5 (*C*H$_{ar}$), 127.9 (*C*H$_{ar}$), 123.3 (N*C*H$_{olef}$), 108.9 (*C*H$_{olef}$), 15.0 (*C*H$_3$).

The NMR spectroscopic data for both isomers are in accordance with the literature.[43]

***tert*-Butyl (*Z*)-prop-1-en-1-ylcarbamate (204a)**



The title compound was prepared according to GP 3 utilizing 28 mg Ni(dppp)Cl_2 (50.0 μmol, 10 mol%), 6.6 mg zinc powder and 32 mg zinc iodide (100 μmol, 20 mol% each). These materials were suspended in 0.3 mL dichloromethane and stirred for 10 min. Then, 0.2 mL of the $HPPh_2$ solution (0.125 M in dichloromethane, 25.0 μmol, 5.0 mol%) were added. After cooling to –30 °C, 79 mg *tert*-

butyl allylcarbamate (0.503 mmol, 1.0 eq) were added and the reaction mixture was stirred for 19 h at –30 °C. After general workup and purification by FC (*n*-pentane/Et_2O 3:1) *tert*-butyl-prop-1-en-1-ylcarbamate (**204a**) was obtained as *Z*/*E*-mixture (81:19) in 79% yield (62 mg, 0.395 mmol) as colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ = δ 6.42 (pt, *J* = 10.4 Hz, 1H, NC*H*$_{olef}$), 6.09 (s, 1H, N*H*), 4.67 – 4.59 (m, 1H, C*H*$_{olef}$), 1.55 (dd, *J* = 6.9, 1.6 Hz, 3H, C*H*$_3$), 1.48 (s, 9H, C(C*H*$_3$)$_3$).

^{13}C NMR (75 MHz, $CDCl_3$) δ = 153.0 (*C*=O), 123.3 (N*C*H$_{olef}$), 102.0 (*C*H$_{olef}$), 80.5 (*C*(CH$_3$)$_3$), 28.4 (C(*C*H$_3$)$_3$), 10.6 (*C*H$_3$).

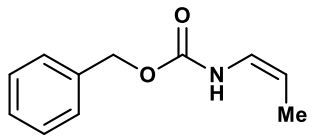
Resolved signals of the minor isomer *tert*-butyl (*E*)-prop-1-en-1-ylcarbamate:

^{1}H NMR (300 MHz, $CDCl_3$) δ = 4.96 – 4.87 (m, 1H, C*H*$_{olef}$), 1.63 (dd, *J* = 6.6, 1.5 Hz, 3H, C*H*$_3$), 1.46 (s, 9H, C(C*H*$_3$)$_3$).

^{13}C NMR (75 MHz, $CDCl_3$) δ = 124.5 (*C*H$_{olef}$), 104.5 (*C*H$_{olef}$), 15.4 (*C*H$_3$).

The NMR spectroscopic data for both isomers are in accordance with the literature.[50]

Benzyl (*Z*)-prop-1-en-1-ylcarbamate (204b)



The title compound was prepared according to GP 3 utilizing 28 mg Ni(dppp)Cl_2 (50.0 μmol, 10 mol%), 6.6 mg zinc powder and 32 mg zinc iodide (100 μmol, 20 mol% each). These materials were suspended in 0.3 mL dichloromethane and stirred for 10 min. Then, 0.2 mL of the $HPPh_2$ solution (0.125 M in dichloromethane, 25.0 μmol, 5.0 mol%) were added. After cooling to –30 °C, 96 mg benzyl allylcarbamate (0.502 mmol, 1.0 eq) were added and the reaction mixture was stirred for 17 h at –30 °C. After general workup and purification by FC (*n*-pentane/Et_2O 4:1) benzyl prop-1-en-1-ylcarbamate (**204b**) was obtained as *Z*/*E*-mixture (81:19) in 69% yield (66 mg, 0.345 mmol) as colorless oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.38 – 7.32 (m, 5H, C*H*$_{ar}$), 6.50 – 6.45 (m, 1H, NC*H*$_{olef}$), 6.37 (br s, 1H, N*H*), 5.16 (s, 2H, C*H*$_2$), 4.70 (dq, *J* = 14.3, 7.2 Hz, 1H, C*H*$_{olef}$), 1.55 (dd, *J* = 7.0, 1.6 Hz, 3H, C*H*$_3$).

^{13}C NMR (125 MHz, $CDCl_3$) δ = 153.7 (*C*=O), 136.1 (*C*$_{q, ar}$), 128.72 (*C*H$_{ar}$), 128.48 (*C*H$_{ar}$), 128.4 (*C*H$_{ar}$), 123.1 (N*C*H$_{olef}$), 103.3 (*C*H$_{olef}$), 67.3 (*C*H$_2$), 10.6 (*C*H$_3$).

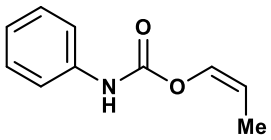
Resolved signals of the minor isomer benzyl (*E*)-prop-1-en-1-ylcarbamate:

^{1}H NMR (500 MHz, $CDCl_3$) δ = 5.03 – 4.97 (m, 1H, C*H*$_{olef}$), 1.65 (d, *J* = 6.4 Hz, 3H, C*H*$_3$).

^{13}C NMR (125 MHz, $CDCl_3$) δ = 153.6 (*C*=O), 128.66 (*C*H$_{ar}$), 128.51 (*C*H$_{ar}$), 128.3 (*C*H$_{ar}$), 124.1 (N*C*H$_{olef}$), 105.9 (*C*H$_{olef}$), 67.1 (*C*H$_2$), 14.8 (*C*H$_3$).

The NMR spectroscopic data for both isomers are in accordance with the literature.[50]

(*Z*)-Prop-1-en-1-yl phenylcarbamate (204c)



The title compound was prepared according to GP 3 utilizing 28 mg Ni(dppp)Cl_2 (50.0 μmol, 10 mol%), 6.6 mg zinc powder and 32 mg zinc iodide (100 μmol, 20 mol% each). These materials were suspended in 0.3 mL dichloromethane and stirred for 10 min. Then, 0.2 mL of the $HPPh_2$ solution (0.125 M in dichloromethane, 25.0 μmol, 5.0 mol%) were added. After cooling to –20 °C, 89 mg allyl phenylcarbamate (0.502 mmol, 1.0 eq) were added and the reaction mixture was stirred for 48 h at –20 °C. After general workup and purification by FC (*n*-pentane/Et_2O 8:1) (*Z*)-prop-1-en-1-yl phenylcarbamate (**204c**) was obtained as *Z*/*E*-mixture (87:13) in 36% yield (32 mg, 0.181 mmol) as white solid.

^{1}H NMR (300 MHz, $CDCl_3$) δ = δ 7.41 (t, *J* = 7.8 Hz, 2H, C*H*$_{ar}$), 7.33 (t, *J* = 7.7 Hz, 2H, C*H*$_{ar}$), 7.10 (t, *J* = 7.3 Hz, 1H, C*H*$_{ar}$), 7.03 – 7.00 (m, 1H, NC*H*$_{olef}$), 6.79 (s, 1H, N*H*), 4.90 (dq, *J* = 13.6, 6.7 Hz, 1H, C*H*$_{olef}$), 1.69 (dd, *J* = 6.9, 1.7 Hz, 3H, C*H*$_3$).

^{13}C NMR (75 MHz, $CDCl_3$) δ = 151.0 (*C*=O), 137.4 (*C*$_{q, ar}$), 135.4 (N*C*H$_{olef}$), 129.3 (*C*H$_{ar}$), 124.1 (*C*H$_{ar}$), 119.1 (*C*H$_{ar}$), 107.3 (*C*H$_{olef}$), 9.8 (*C*H$_3$).

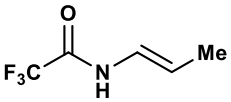
Resolved signals of the minor isomer (*E*)-prop-1-en-1-yl phenylcarbamate:

^{1}H NMR (300 MHz, $CDCl_3$) δ = 5.38 (dq, *J* = 12.4, 6.9 Hz, 1H, C*H*$_{olef}$).

^{13}C NMR (75 MHz, $CDCl_3$) δ = 136.4 (N*C*H$_{olef}$), 12.4 (*C*H$_3$).

The NMR spectroscopic data for both isomers are in accordance with the literature.[151]

(*E*)-2,2,2-Trifluoro-*N*-(prop-1-en-1-yl)acetamide (206a)



The title compound was prepared according to GP 3 utilizing 14 mg Ni(dppp)Cl_2 (25.0 μmol, 10 mol%), 3.3 mg zinc powder and 16 mg zinc iodide (50 μmol, 20 mol% each). These materials were suspended in

0.15 mL dichloromethane and stirred for 10 min. Then, 0.1 mL of the $HPPh_2$ solution (0.125 M in dichloromethane, 12.5 μmol, 5.0 mol%) and 33 mg *N*-allyl-2,2,2-trifluoroacetamide (0.215 mmol, 1.0 eq) were added at ambient temperature and the reaction mixture was stirred for 2 d. Additionally, 7 mg $Ni(dppp)Cl_2$ (12.5 μmol, 5.0 mol%), 1.7 mg zinc powder and 8 mg zinc iodide (25 μmol, 10 mol% each) and 0.05 mL of the $HPPh_2$ solution (0.125 M in dichloromethane, 6.0 μmol, 2.5.0 mol%) were added to the reaction mixture after 16 h at ambient temperature to complete the conversion of the starting material. After general workup and purification by FC (*n*-pentane/Et_2O 2:1) 2,2,2-trifluoro-*N*-(prop-1-en-1-yl)acetamide (**206a**) was obtained as *Z*/*E*-mixture (15:85) in 64% yield (21 mg, 0.137 mmol) as colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ = δ 7.77 (s, 1H, N*H*), 6.65 (t, *J* = 11.6 Hz, 1H, NCH_{olef}), 5.50 (qd, *J* = 14.1 Hz, 7.1 Hz, 1H, CH_{olef}), 1.73 (dd, *J* = 6.9, 1.4 Hz, 3H, CH_3).

^{13}C NMR (75 MHz, $CDCl_3$) δ = 121.0 (N*C*H_{olef}), 114.2 (*C*H_{olef}), 15.0 (*C*H_3). *C*=O and *C*F_3 not detectable.

^{19}F NMR (283 MHz, $CDCl_3$) δ = –75.77 (s, 3F, CF_3).

IR (neat) 3289, 3214, 3078, 1698, 1542, 1439, 1300, 1273, 1215, 1157, 947, 871, 774, 520.

HRMS (ESI) *m*/*z* $[M+Na]^+$ calculated for $C_5H_6F_3NONa$: 176.0299; found: 176.0299.

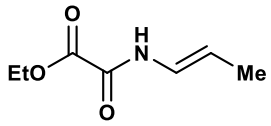
Resolved signals of the minor isomer (*Z*)-2,2,2-trifluoro-N-(prop-1-en-1-yl)acetamide:

^{1}H NMR (300 MHz, $CDCl_3$) δ = 5.16 (dq, *J* = 8.2, 5.7 Hz, 1H, CH_{olef}), 1.69 (dd, *J* = 7.1, 1.5 Hz, 3H, CH_3).

^{13}C NMR (75 MHz, $CDCl_3$) δ = 117.8 (N*C*H_{olef}), 111.5 (*C*H_{olef}), 11.1 (*C*H_3).

^{19}F NMR (283 MHz, $CDCl_3$) δ = –75.70 (s, 3F, CF_3).

Ethyl (*E*)-2-oxo-2-(prop-1-en-1-ylamino)acetate (206b)



The title compound was prepared according to GP 3 utilizing 28 mg $Ni(dppp)Cl_2$ (50.0 μmol, 10 mol%), 6.6 mg zinc powder and 32 mg zinc iodide (100 μmol, 20 mol% each). These materials were suspended in 0.3 mL dichloromethane and stirred for 10 min. Then, 0.2 mL of the $HPPh_2$ solution (0.125 M in dichloromethane, 25.0 μmol, 5.0 mol%) and 79 mg ethyl-2-(allylamino)-2-oxoacetate (0.503 mmol, 1.0 eq) were added at ambient temperature and the reaction mixture was stirred for 95 h. After general workup and purification by FC (*n*-pentane/Et_2O 2:1) ethyl-2-oxo-2-

(prop-1-en-1-ylamino)acetate (**206b**) was obtained as *Z*/*E*-mixture (8:92) in 29% yield (23 mg, 0.150 mmol) as colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.52 (br s, 1H, N*H*), 6.73 – 6.64 (m, 1H, NC*H*$_{olef}$), 5.50 – 5.38 (m, 1H, C*H*$_{olef}$), 4.35 (q, *J* = 7.1 Hz, 2H, C*H*$_2$), 1.71 (dd, *J* = 6.8, 1.7 Hz, 3H, C*H*$_3$), 1.37 (t, *J* = 7.1 Hz, 3H, CH_2C*H*$_3$).

^{13}C NMR (75 MHz, $CDCl_3$) δ 160.7 (*C*=O), 153.2 (*C*=O), 122.2 (N*C*H$_{olef}$), 112.7 (*C*H$_{olef}$), 63.5 (*C*H$_2$), 15.0 (*C*H$_3$), 14.1 (CH_2*C*H$_3$).

IR (neat) 3245, 3185, 2991, 2964, 2921, 2856, 1734, 1667, 1578, 1516, 1475, 1444, 1393, 1367, 1317, 1258, 1219, 1205, 1154, 1112, 1092, 1017, 958, 921, 861, 808, 782, 742, 697, 603, 533, 482, 455, 402.

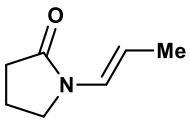
HRMS (ESI) calculated for $C_7H_{12}NO_3$: *m*/*z* = 158.0812; found *m*/*z* = 158.0812.

Resolved signals of the minor isomer ethyl (*Z*)-2-oxo-2-(prop-1-en-1-ylamino)acetate:

^{1}H NMR (300 MHz, $CDCl_3$) δ 5.09 – 4.99 (m, 1H, C*H*$_{olef}$).

^{13}C NMR (75 MHz, $CDCl_3$) δ 11.1 (*C*H$_3$).

(*E*)-1-(Prop-1-en-1-yl)pyrrolidin-2-one (210a)



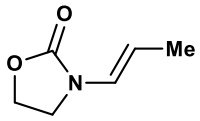
The title compound was prepared according to GP 3 utilizing 28 mg Ni(dppp)Cl_2 (50.0 μmol, 10 mol%), 6.6 mg zinc powder and 32 mg zinc iodide (100 μmol, 20 mol% each). These materials were suspended in 0.3 mL dichloromethane and stirred for 10 min. Then, 0.2 mL of the $HPPh_2$ solution (0.125 M in dichloromethane, 25.0 μmol, 5.0 mol%) were added. 62 mg 1-allylpyrrolidin-2-one (0.495 mmol, 1.0 eq) were added at ambient temperature and the reaction mixture was stirred for 24 h. After general workup and purification by FC (*n*-pentane/Et_2O 2:1) 1-(prop-1-en-1-yl)pyrrolidin-2-one (**210a**) was obtained as single *E*-isomer in 98% yield (61 mg, 0.487 mmol) as colorless liquid.

^{1}H NMR (300 MHz, $CDCl_3$) δ = 6.88 (d, *J* = 14.1 Hz, 1H, NC*H*$_{olef}$), 4.94 (qd, *J* = 14.1, 7.4 Hz, 1H, C*H*$_{olef}$), 3.48 (t, *J* = 7.2 Hz, 2H, C*H*$_2$), 2.46 (t, *J* = 8.1 Hz, 2H, C*H*$_2$), 2.12 – 2.02 (m, 2H, C*H*$_2$), 1.72 (dd, *J* = 6.7 1.3 Hz, 3H, C*H*$_3$).

^{13}C NMR (75 MHz, $CDCl_3$) δ = 172.7 (*C*=O), 124.6 (N*C*H$_{olef}$), 106.9 (*C*H$_{olef}$), 45.4 (*C*H$_2$), 31.4 (*C*H$_2$), 17.6 (*C*H$_2$), 15.3 (*C*H$_3$).

The NMR spectroscopic data are in accordance with the literature.[50]

(*E*)-3-(Prop-1-en-1-yl)oxazolidin-2-one (210b)



The title compound was prepared according to GP 3 utilizing 14 mg Ni(dppp)Cl_2 (25.0 µmol, 10 mol%), 3.3 mg zinc powder and 16 mg zinc iodide (50 µmol, 20 mol% each). These materials were suspended in 0.15 mL dichloromethane and stirred for 10 min. Then, 0.1 mL of the $HPPh_2$ solution (0.125 M in dichloromethane, 12.5 µmol, 5.0 mol%) were added. 32 mg 3-allyloxazolidin-2-one (0.250 mmol, 1.0 eq) were added at ambient temperature and the reaction mixture was stirred for 16 h at ambient temperature. After general workup and purification by FC (*n*-pentane/EtOAc 2:1) 3-(prop-1-en-1-yl)oxazolidin-2-one (**210b**) was obtained as *Z*/*E*-mixture (6:94) in 94% yield (30 mg, 0.236 mmol) as colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ = δ 6.65 (d, *J* = 14.5 Hz, 1H, NCH_{olef}), 4.81 (dt, *J* = 14.1, 7.2 Hz, 1H, CH_{olef}), 4.42 (t, *J* = 8.0 Hz, 2H, CH_2), 3.67 (t, *J* = 8.1 Hz, 2H, CH_2), 1.72 (dd, *J* = 7.0, 1.0 Hz, 3H, CH_3).

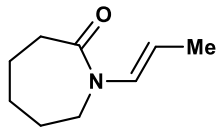
^{13}C NMR (75 MHz, $CDCl_3$) δ = 155.5 (*C*=O), 124.8 (N*C*H$_{olef}$), 105.8 (*C*H$_{olef}$), 62.2 (*C*H$_2$), 42.8 (*C*H$_2$), 15.0 (*C*H$_3$).

Resolved signals of the minor isomer (*Z*)-3-(prop-1-en-1-yl)oxazolidin-2-one:

^{1}H NMR (300 MHz, $CDCl_3$) δ = 6.23 (d, *J* = 7.6 Hz, 1H, NCH_{olef}), 5.02 – 4.91 (m, 1H, CH_{olef}), 3.98 (t, *J* = 7.9 Hz, 2H, CH_2).

The NMR spectroscopic data are in accordance with the literature.[44]

(*E*)-1-(Prop-1-en-1-yl)azepan-2-one (210c)



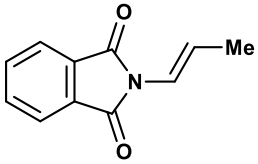
The title compound was prepared according to GP 3 utilizing 28 mg Ni(dppp)Cl_2 (50.0 µmol, 10 mol%), 6.6 mg zinc powder and 32 mg zinc iodide (100 µmol, 20 mol% each). These materials were suspended in 0.3 mL dichloromethane and stirred for 10 min. Then, 0.2 mL of the $HPPh_2$ solution (0.125 M in dichloromethane, 25.0 µmol, 5.0 mol%) were added. 77 mg 1-allylazepan-2-one (0.502 mmol, 1.0 eq) were added at ambient temperature and the reaction mixture was stirred for 16 h. After general workup and purification by FC (*n*-pentane/EtOAc 2:1) 1-(prop-1-en-1-yl)azepan-2-one (**210c**) was obtained as single *E*-isomer in 77% yield (59 mg, 0.385 mmol) as white solid.

^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.11 (dd, *J* = 14.6, 1.3 Hz, 1H, NC*H*$_{olef}$), 5.10 – 4.98 (m, 1H, C*H*$_{olef}$), 3.55 (t, *J* = 4.7 Hz, 2H, C*H*$_2$), 2.59 (t, *J* = 5.4 Hz, 2H, C*H*$_2$), 1.73 – 1.70 (m, 6H, C*H*$_2$), 1.68 – 1.63 (m, 3H, C*H*$_3$).

^{13}C NMR (75 MHz, $CDCl_3$) δ = 174.0 (*C*=O), 127.8 (N*C*H$_{olef}$), 106.0 (*C*H$_{olef}$), 45.8 (*C*H$_2$), 37.4 (*C*H$_2$), 29.7 (*C*H$_2$), 27.6 (*C*H$_2$), 23.6 (*C*H$_2$), 15.4 (*C*H$_3$).

The NMR spectroscopic data are in accordance with the literature.[46]

(*E*)-2-(Prop-1-en-1-yl)isoindoline-1,3-dione (210d)



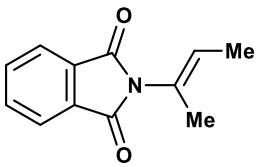
The title compound was prepared according to GP 3 utilizing 32 mg $Ni(dppp)Br_2$ (50.0 μmol, 10 mol%), 6.6 mg zinc powder and 32 mg zinc iodide (100 μmol, 20 mol% each). These materials were suspended in 0.3 mL dichloromethane and stirred for 10 min. Then, 0.2 mL of the $HPPh_2$ solution (0.125 M in dichloromethane, 25.0 μmol, 5.0 mol%) and 94 mg 2-allylisoindoline-1,3-dione (0.502 mmol, 1.0 eq) were added at ambient temperature and the reaction mixture was stirred for 18 h. After general workup and purification by FC (*n*-pentane/MTBE 20:1) 2-(prop-1-en-1-yl)isoindoline-1,3-dione (**210d**) was obtained as single *E*-isomer in 85% yield (80 mg, 0.426 mmol) as yellow solid.

^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.87 – 7.83 (m, 2H, C*H*$_{ar}$), 7.75 – 7.70 (m, 2H, C*H*$_{ar}$), 6.64 – 6.53 (m, 2H, C*H*$_{olef}$), 1.84 (d, *J* = 5.0 Hz, 3H, C*H*$_3$).

^{13}C NMR (75 MHz, $CDCl_3$) δ = 168.8 (*C*=O), 134.4 (*C*H$_{ar}$), 131.9 (*C*$_{q, ar}$), 123.6 (*C*H$_{ar}$), 118.5 (*C*H$_{olef}$), 118.3 (*C*H$_{olef}$), 16.4 (*C*H$_3$).

The NMR spectroscopic data are in accordance with the literature.[44]

(*E*)-2-(But-2-en-2-yl)isoindoline-1,3-dione (210e)



The title compound was prepared according to GP 3 utilizing 14 mg $Ni(dppp)Cl_2$ (25.0 μmol, 10 mol%), 3.3 mg zinc powder and 16 mg zinc iodide (50 μmol, 20 mol% each). These materials were suspended in 0.15 mL dichloromethane and stirred for 10 min. Then, 0.1 mL of the $HPPh_2$ solution (0.125 M in dichloromethane, 12.5 μmol, 5.0 mol%) were added. After cooling to 0 °C, 50 mg 2-(but-3-en-2-yl)isoindoline-1,3-dione (0.250 mmol, 1.0 eq) were added and the reaction mixture was stirred for 3 d at 0 °C. After general workup and purification by FC (*n*-pentane/EtOAc 9:1) 2-

(but-2-en-2-yl)isoindoline-1,3-dione (**210e**) was obtained as *Z*/*E*-mixture (33:67) in 70% yield (35 mg, 0.170 mmol) as colorless oily solid.

^{1}H NMR (300 MHz, $CDCl_3$) δ = δ 7.90 – 7.83 (m, 2H, C*H*$_{ar}$), 7.77 – 7.71 (m, 2H, C*H*$_{ar}$), 5.58 (q, *J* = 7.0 Hz, 1H, C*H*$_{olef}$), 1.97 (s, 3H, C*H*$_3$), 1.83 (d, *J* = 7.0 Hz, 3H, C*H*$_3$).

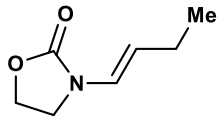
^{13}C NMR (75 MHz, $CDCl_3$) δ = 167.7 (*C*=O), 134.2 (*C*H$_{ar}$), 132.2 (*C*$_{q, olef}$), 127.2 (*C*$_{q, ar}$), 127.0 (*C*H$_{olef}$), 123.6 (*C*H$_{ar}$), 15.7 (*C*H$_3$), 13.4 (*C*H$_3$).

IR (neat) 3464, 2977, 2924, 2861, 1715, 1699, 1308, 1286, 1121, 1078, 885, 713, 530.

HRMS (ESI) *m*/*z* $[M+Na]^+$ calculated for $C_{12}H_{11}NO_2Na$: 224.0682; found: 224.0682.

Resolved signals of the minor isomer (*Z*)-2-(but-2-en-2-yl)isoindoline-1,3-dione:
^{1}H NMR (300 MHz, $CDCl_3$) δ = 5.81 (q, *J* = 6.9 Hz, 1H, C*H*$_{olef}$), 2.00 (s, 3H, C*H*$_3$), 1.53 (d, *J* = 6.8 Hz, 3H, C*H*$_3$).
^{13}C NMR (75 MHz, $CDCl_3$) δ = 167.1 (*C*=O), 134.1 (*C*H$_{ar}$), 132.4 (*C*$_{q, olef}$), 127.2 (*C*H$_{olef}$), 126.0 (*C*H$_{ar}$), 123.5 (*C*H$_{ar}$), 21.1 (*C*H$_3$), 13.5 (*C*H$_3$).

(*E*)-3-(But-1-en-1-yl)oxazolidin-2-one (218)



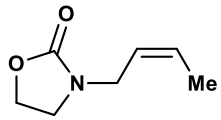
The title compound was prepared according to GP 3 utilizing 28 mg Ni(dppp)Cl_2 (50.0 μmol, 10 mol%), 6.6 mg zinc powder and 32 mg zinc iodide (100 μmol, 20 mol% each). These materials were suspended in 0.3 mL dichloromethane and stirred for 10 min. Then, 0.2 mL of the $HPPh_2$ solution (0.125 M in dichloromethane, 25.0 μmol, 5.0 mol%) and 71 mg 3-(but-3-en-1-yl)oxazolidin-2-one (0.503 mmol, 1.0 eq) were added at ambient temperature and the reaction mixture was stirred for 16 h. After general workup and purification by FC (*n*-pentane/EtOAc 1:1) 3-(but-1-en-1-yl)oxazolidin-2-one (**218**) was obtained as single *E*-isomer in 82% yield (58 mg, 0.411 mmol) as colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ = 6.65 (d, *J* = 14.2 Hz, 1H, NC*H*$_{olef}$), 4.86 (dt, *J* = 14.4, 7.2 Hz, 1H, C*H*$_{olef}$), 4.42 (t, *J* = 8.1 Hz, 2H, C*H*$_2$), 3.68 (t, *J* = 8.0 Hz, 2H, C*H*$_2$), 2.09 (dq, *J* = 7.1, 1.2 Hz, 2H, C*H*$_2$), 1.02 (t, *J* = 7.4 Hz, 3H, C*H*$_3$).

^{13}C NMR (75 MHz, $CDCl_3$) δ = 155.6 (*C*=O), 123.5 (N*C*H$_{olef}$), 113.5 (*C*H$_{olef}$), 62.2 (*C*H$_2$), 42.8 (*C*H$_2$), 23.1 (*C*H$_2$), 14.6 (*C*H$_3$).

The NMR spectroscopic data are in accordance with the literature.[152]

(*Z*)-3-(But-2-en-1-yl)oxazolidin-2-one (219)



The title compound was prepared according to GP 3 utilizing 14 mg Ni(dppp)Cl_2 (25.0 μmol, 10 mol%), 3.3 mg zinc powder and 16 mg zinc iodide (50 μmol, 20 mol% each). These materials were suspended in 0.15 mL dichloromethane and stirred for 10 min. Then, 0.1 mL of the $HPPh_2$ solution (0.125 M in dichloromethane, 12.5 μmol, 5.0 mol%) were added. After cooling to –10 °C 36 mg 3-(but-3-en-1-yl)oxazolidin-2-one (0.251 mmol, 1.0 eq) were added at ambient temperature and the reaction mixture was stirred for 16 h at – 10 °C. After general workup and purification by FC (*n*-pentane/EtOAc 1:1) (*Z*)-3-(but-2-en-1-yl)oxazolidin-2-one (**219**) was obtained as *Z*/*E*-mixture (84:16) in 83% yield (30 mg, 0.208 mmol) as colorless oil. The product contained 11% of remaining starting material.

^{1}H NMR (300 MHz, $CDCl_3$) δ = 5.79 – 5.64 (m, 1H, CH_{olef}), 5.45 – 5.34 (m, 1H, CH_{olef}), 4.31 (t, *J* = 8.0 Hz, 2H, CH_2), 3.92 (d, *J* = 7.2 Hz, 2H, CH_2), 3.51 (t, *J* = 8.0 Hz, 2H, CH_2), 1.70 (dd, *J* = 7.0, 0.7 Hz, 3H, CH_3).

^{13}C NMR (75 MHz, $CDCl_3$) δ = 158.5 (*C*=O), 129.6 (*C*H_{olef}), 123.9 (*C*H_{olef}), 61.8 (*C*H_2), 44.2 (*C*H_2), 40.7 (*C*H_2), 13.0 (*C*H_3).

IR (neat) 2919, 1737, 1484, 1424, 1255, 1192, 1066, 1034, 762, 726.

HRMS (ESI) *m*/*z* $[M+Na]^+$ calculated for $C_7H_{11}NO_2Na$: 164.0682; found: 164.0682.

Resolved signals of the minor isomer (*E*)-3-(but-2-en-1-yl)oxazolidin-2-one:

^{1}H NMR (300 MHz, $CDCl_3$) δ = 3.80 (d, *J* = 7.0 Hz, 2H, CH_2), 1.26 (d, *J* = 7.9 Hz, 3H, CH_3).

^{13}C NMR (75 MHz, $CDCl_3$) δ = 60.5 (*C*H_2), 44.6 (*C*H_2), 17.9 (*C*H_3).

Resolved signals of the starting material 3-(but-3-en-1-yl)oxazolidin-2-one:

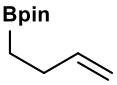
^{1}H NMR (300 MHz, $CDCl_3$) δ = 5.15 – 5.06 (m, 2H, C$H_{2,\ olef}$), 3.34 (t, *J* = 7.1 Hz, 2H, CH_2), 2.33 (pq, *J* = 7.2 Hz, 2H, CH_2).

^{13}C NMR (75 MHz, $CDCl_3$) δ = 43.6 (*C*H_2), 32.1 (*C*H_2).

5.5 Isomerization/Allylboration Sequence

5.5.1 Synthesis of Homoallyl Boronic Esters

2-(But-3-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (132)



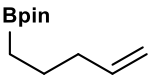
The title compound was prepared according to GP 4. First, 875 mg magnesium turnings (36.0 mmol, 1.2 eq) were suspended in 30 mL Et_2O and 4.05 g 4-bromobut-1-ene (30.0 mmol, 1.0 eq) were added at ambient temperature. The reaction mixture was stirred at 50 °C for 1 h and then cooled to −78 °C. At this temperature, 8.31 mL B(O*i*Pr)$_3$ (36.0 mmol, 1.2 eq) were added and the reaction mixture was stirred for 30 min. The reaction was quenched with 1 M aqueous HCl, the aqueous layer was extracted with Et_2O, dried over $MgSO_4$ and filtered. The solvent was removed under reduced pressure, the residue was taken up in 100 mL of the solvent mixture *n*-pentane/ Et_2O (4:1) and 3.55 g pinacol (30 mmol, 1.0 eq) were added. The reaction was stirred for 3 d at ambient temperature, the solvent was evaporated, and the residue was purified by FC (*n*-pentane/Et_2O 25:1) to give 2-(but-3-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**132**) in 99% yield (5.38 g, 29.6 mmol) as colorless liquid.

^{1}H NMR (300 MHz, $CDCl_3$) δ 5.95 – 5.82 (m, 1H, C*H*$_{olef}$), 4.99 (dd, *J* = 17.1, 1.8 Hz, 1H, C*H*$_{olef}$), 4.90 (dd, *J* = 10.5, 1.6 Hz, 1H, C*H*$_{olef}$), 2.23 – 2.13 (m, 2H, C*H*$_2$), 1.24 (s, 12H, C*H*$_{3,\ pin}$), 0.89 (t, *J* = 7.8 Hz, 2H, C*H*$_2$).

^{13}C NMR (75 MHz, $CDCl_3$) δ 140.9 (*C*H$_{olef}$), 113.3 (*C*H$_{olef}$), 83.2 (C$_{q,\ pin}$), 28.1 (*C*H$_2$), 25.0 (*C*H$_{3,\ pin}$). pinB–*C*H$_2$ not detectable.

The NMR spectroscopic data are in accordance with the literature.[79]

4,4,5,5-Tetramethyl-2-(pent-4-en-1-yl)-1,3,2-dioxaborolane (222a)



The title compound was prepared according to GP 4. First, 583 mg magnesium turnings (24.0 mmol, 1.2 eq) were suspended in 30 mL Et_2O and 2.89 g 5-bromopent-1-ene (20.0 mmol, 1.0 eq) were added at ambient temperature. The reaction mixture was stirred at 50 °C for 1 h and then cooled to −78 °C. At this temperature, 4.62 mL B(O*i*Pr)$_3$ (20.0 mmol, 1.0 eq) were added and the reaction mixture was stirred for 30 min. The reaction was quenched with 1 M aqueous HCl, the aqueous layer was extracted with Et_2O, dried over $MgSO_4$ and filtered. The solvent was removed under reduced pressure, the residue was taken up in 80 mL of the solvent mixture *n*-pentane/Et_2O (4:1) and 2.36 g pinacol (20.0 mmol, 1.0 eq) were added. The reaction was stirred for 3 d at ambient temperature, the solvent was

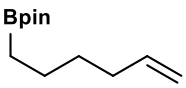
evaporated and the residue was purified by FC (*n*-pentane/Et_2O 25:1) to give 4,4,5,5-tetramethyl-2-(pent-4-en-1-yl)-1,3,2-dioxaborolane (**222a**) in 67% yield (2.62 g, 13.3 mmol) as colorless liquid.

^{1}H NMR (300 MHz, $CDCl_3$) δ = 5.79 (ddd, *J* = 16.9, 10.3, 6.6 Hz, 1H, C*H*$_{olef}$), 4.97 (dd, *J* = 17.2, 1.6 Hz, 1H, C*H*$_{olef}$), 4.92 (d, *J* = 17.2 Hz, 1H, C*H*$_{olef}$), 2.04 (dd, *J* = 7.5, 7.2 Hz, 2H, C*H*$_2$), 1.50 (p, *J* = 7.6 Hz, 2H, C*H*$_2$), 1.24 (s, 12H, C*H*$_{3,\ pin}$), 0.78 (t, *J* = 7.8 Hz, 2H, C*H*$_2$).

^{13}C NMR (75 MHz, $CDCl_3$) δ = 139.1 (*C*H$_{olef}$), 114.6 (*C*H$_{2,\ olef}$), 83.0 (*C*$_{q,\ pin}$), 36.5 (*C*H$_2$), 24.9 (*C*H$_{3,\ pin}$), 23.5 (*C*H$_2$), 10.4 (br s, B-*C*H$_2$).

The NMR spectroscopic data are in accordance with the literature.[153]

2-(Hex-5-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (222b)



The title compound was prepared according to GP 4. First, 583 mg magnesium turnings (24.0 mmol, 1.2 eq) were suspended in 20 mL THF and 2.76 mL 6-bromohex-1-ene (20.0 mmol, 1.0 eq) were added at ambient temperature. The reaction mixture was stirred at 40 °C for 1 h and then cooled to −78 °C. At this temperature, 5.54 mL B(O*i*Pr)$_3$ (24.0 mmol, 1.2 eq) were added and the reaction mixture was stirred for 15 min. The reaction was quenched with 1 M aqueous HCl, the aqueous layer was extracted with Et_2O, dried over $MgSO_4$ and filtered. The solvent was removed under reduced pressure, the residue was taken up in 100 mL of the solvent mixture *n*-pentane/ Et_2O (4:1) and 2.84 g pinacol (24.0 mmol, 1.2 eq) were added. The reaction was stirred for 3 d at ambient temperature, the solvent was evaporated, and the residue was purified by FC (*n*-pentane/Et_2O 70:1) to give 2-(hex-5-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**222b**) in 55% yield (2.29 g, 11.0 mmol) as colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ 5.88 – 5.74 (m, 1H, C*H*$_{olef}$), 5.02 – 4.89 (m, 2H, C*H*$_{2,\ olef}$), 2.08 – 2.01 (m, 2H, C*H*$_2$), 1.45 – 1.37 (m, 4H, C*H*$_2$), 1.24 (s, 12H, *H*$_{pin}$), 0.78 (t, *J* = 7.35 Hz, 2H, C*H*$_2$).

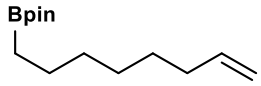
^{13}C NMR (75 MHz, $CDCl_3$) δ 139.4 (*C*H$_{olef}$), 114.2 (*C*H$_{2,\ olef}$), 83.1 (*C*$_{q,\ pin}$), 33.8 (*C*H$_2$), 31.9 (*C*H$_2$), 25.0 (*C*$_{pin}$), 23.8 (B-*C*H$_2$).

^{11}B NMR (96 MHz, $CDCl_3$) δ 34.0 (*B*pin).

IR (neat) 3076, 2978, 2927, 2860, 1640, 1462, 1407, 1371, 1317, 1272, 1224, 1144, 1111, 990, 967, 908, 880, 846, 805, 724, 672, 633, 577, 543, 439, 397.

HRMS (EI) calculated for $C_{12}H_{23}BO_2$: *m*/*z* = 210.1791; found *m*/*z* = 210.1792.

4,4,5,5-Tetramethyl-2-(oct-7-en-1-yl)-1,3,2-dioxaborolane (222c)



The title compound was prepared according to GP 4. First, 583 mg magnesium turnings (24.0 mmol, 1.2 eq) were suspended in 20 mL THF and 3.35 mL 8-bromooct-1-ene (20.0 mmol, 1.0 eq) were added at ambient temperature. The reaction mixture was stirred at 50 °C for 2 h and 15 min and then cooled to –78 °C. At this temperature, 5.54 mL B(O*i*Pr)$_3$ (24.0 mmol, 1.2 eq) were added and the reaction mixture was stirred for 15 min. The reaction was quenched with 1 M aqueous HCl, the aqueous layer was extracted with Et_2O, dried over $MgSO_4$ and filtered. The solvent was removed under reduced pressure, the residue was taken up in 100 mL of the solvent mixture *n*-pentane/ Et_2O (4:1) and 2.84 g pinacol (24.0 mmol, 1.2 eq) were added. The reaction was stirred for 3 d at ambient temperature, the solvent was evaporated, and the residue was purified by FC (*n*-pentane/Et_2O 70:1) to give 4,4,5,5-tetramethyl-2-(oct-7-en-1-yl)-1,3,2-dioxaborolane (**222c**) in 71% yield (3.40 g, 14.3 mmol) as colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ = 5.88 – 5.74 (m, 1H, C*H*$_{olef}$), 5.02 – 4.90 (m, 2H, C*H*$_{2,\ olef}$), 2.06 – 2.00 (m, 2H, C*H*$_2$), 1.42 – 1.26 (m, 8H, C*H*$_2$), 1.24 (s, 12H, C*H*$_{3,\ pin}$), 0.77 (t, *J* = 7.5 Hz, 2H, C*H*$_2$).

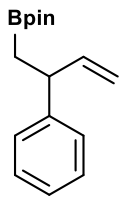
^{13}C NMR (75 MHz, $CDCl_3$) δ = 139.5 (*C*H$_{olef}$), 114.2 (*C*H$_{2,\ olef}$), 83.0 (*C*$_{q,\ pin}$), 34.0 (*C*H$_2$), 32.4 (*C*H$_2$), 29.1 (*C*H$_2$), 29.1 (*C*H$_2$), 25.0 (*C*H$_{3,\ pin}$), 24.1 (B*C*H$_2$).

^{11}B NMR (96 MHz, $CDCl_3$) δ 34.0 (*B*pin).

IR (neat) 3076, 2978, 2925, 2855, 2028, 1640, 1464, 1407, 1371, 1316, 1271, 1214, 1144, 1111, 992, 968, 908, 877, 846, 804, 721, 672, 634, 577, 545, 519, 440, 406.

EI-HRMS calculated for $C_{14}H_{27}BO_2$: *m*/*z* = 238.2105; found *m*/*z* = 238.2109.

4,4,5,5-Tetramethyl-2-(2-phenylbut-3-en-1-yl)-1,3,2-dioxaborolane (227)



The title compound was prepared according to GP 5. First, 160 mg magnesium turnings (6.58 mmol, 1.2 eq), 740 mg pinacolborane (5.80 mmol, 1.0 eq) and 0.8 mL triethylamine (5.80 mmol, 1.0 eq) were suspended in 15 mL THF. At ambient temperature 2.10 g (1-bromobut-3-en-2-yl)benzene (5.71 mmol, 1.0 eq) were added and the reaction mixture was stirred overnight at 66 °C. The reaction was quenched with 0.2 M aqueous HCl, the aqueous layer was extracted with Et_2O, dried over $MgSO_4$ and filtered. The

solvent was removed under reduced pressure and the crude product was purified by FC (*n*-pentane/Et_2O 20:1) to give 4,4,5,5-tetramethyl-2-(2-phenylbut-3-en-1-yl)-1,3,2-dioxaborolane (**227**) in 50% yield (743 mg, 2.88 mmol) as colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.29 – 7.21 (m, 5H, CH_{ar}), 6.07 – 5.95 (m, 1H, CH_{olef}), 5.07 – 4.91 (m, 2H, C$H_{2,\ olef}$), 3.61 (q, *J* = 8.46 Hz, 1H, C*H*), 1.19 (d, *J* = 6.36 Hz, 2H, CH_2), 1.14 (s, 12H, C$H_{3,\ pin}$).

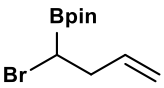
^{13}C NMR (75 MHz, $CDCl_3$) δ 145.9 ($C_{q,\ ar}$), 143.9 (*C*H$_{olef}$), 128.5 (*C*H$_{ar}$), 127.6 (*C*H$_{ar}$), 126.2 (*C*H$_{ar}$), 112.9 (*C*H$_{2,\ olef}$), 83.3 ($C_{q,\ pin}$), 45.2 (*C*H), 24.8 (*C*H$_{3,\ pin}$), 24.9 (B*C*H$_2$).

^{11}B NMR (96 MHz, $CDCl_3$) δ 33.7 (*B*pin).

IR (neat) 3062, 3027, 2977, 2930, 1637, 1601, 1492, 1480, 1467, 1452, 1388, 1362, 1323, 1270, 1213, 1164, 1142, 1112, 1071, 1030, 994, 967, 911, 885, 846, 825, 779, 749, 698, 671, 578, 554, 510, 420.

HRMS (EI) calculated for $C_{16}H_{23}BO_2$: *m*/*z* = 258.1791; found *m*/*z* = 258.1786.

2-(1-Bromobut-3-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (223)



According to a procedure of Hoffmann,[128] 6.57 g 2-(dibromomethyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (21.9 mmol, 1.0 eq) were dissolved in 50 mL anhydrous THF. At −100 °C, 21.9 mL allylmagnesiumbromide solution (1.0 m in Et_2O, 21.9 mmol, 1.0 eq) were added and the reaction was warmed very slowly to ambient temperature (overnight) with the Schlenk flask remaining inside the cooling bath. The reaction mixture was quenched with H_2O and the aqueous layer was extracted three times with Et_2O, the organic layer was dried over $MgSO_4$, filtered and the solvent was evaporated. The crude product was purified by FC (*n*-pentane/Et_2O 25:1) to give 2-(1-bromobut-3-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**223**) in 62% yield (3.55g, 13.6 mmol) as colorless liquid.

^{1}H NMR (300 MHz, $CDCl_3$) δ 5.88 – 5.72 (m, 1H, CH_{olef}), 5.15 – 5.07 (m, 2H, C$H_{2,\ olef}$), 3.31 (t, *J* = 7.9 Hz, 1H, C*H*), 2.74 – 2.56 (m, 2H, CH_2), 1.28 (s, 12H, C$H_{3,\ pin}$).

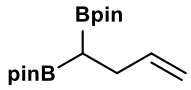
^{13}C NMR (75 MHz, $CDCl_3$) δ 135.8 (*C*H$_{olef}$), 117.6 (*C*H$_{2,\ olef}$), 84.5 ($C_{q,\ pin}$), 38.4 (*C*H$_2$), 24.6 (*C*H$_{3,\ pin}$). B*C*H$_2$ not detectable.

^{11}B NMR (96 MHz, $CDCl_3$) δ 33.8 (*B*pin).

IR (neat) 2979, 2931, 1641, 1379, 1372, 1347, 1272, 1250, 1167, 1141, 994, 966, 920, 844, 673, 606, 577.

HRMS (EI) calculated for $C_{10}H_{18}BBrO_2$: *m*/*z* = 260.0583; found *m*/*z* = 260.0597.

2,2'-(But-3-en-1,1-diyl)-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (224)



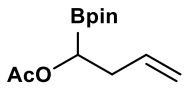
According to a procedure of Meek,[154] 1.72 mL di*iso*propylamine (12.3 mmol, 1.03 eq) were dissolved in 41 mL anhydrous THF and 4.9 mL *n*-BuLi solution (2.5 M in *n*-hexane, 12.3 mmol, 1.03 eq) were added at 0 °C. After stirring for 30 min at 0 °C 3.19 g bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methane (11.9 mmol, 1.0 eq) were added and the reaction mixture was stirred for another 10 min. Then, 2.5 mL allylbromide (29.3 mmol, 2.46 eq) were added. The reaction was warmed to ambient temperature and stirred overnight. The reaction was quenched with sat. aqueous NH_4Cl solution and the aqueous layer was extracted three times with Et_2O, dried over $MgSO_4$, filtered and the solvent was evaporated. The crude product was purified by FC (*n*-pentane/Et_2O 30:1) to give 2,2'-(but-3-en-1,1-diyl)-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (**224**) in 27% yield (980 mg, 3.18 mmol) as pale yellow sticky oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ 5.95 – 5.80 (m, 1H, CH_{olef}), 5.04 – 4.83 (m, 2H, C$H_{2,\ olef}$), 2.29 (ddt, *J* = 8.3, 6.5, 1.5 Hz, 2H, CH_2), 1.22 (s, 24H, C$H_{3,\ pin}$), 0.84 (t, *J* = 8.1 Hz, 1H, C*H*).

^{13}C NMR (75 MHz, $CDCl_3$) δ 140.9 (*C*H_{olef}), 113.3 (*C*$H_{2,\ olef}$), 83.1 ($C_{q,\ pin}$), 27.7 (*C*H_2), 25.0 (*C*$H_{3,\ pin}$), 24.7 (*C*$H_{3,\ pin}$). B_2*C*H not detectable.

The NMR spectroscopic data are in accordance with the literature.[154]

1-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)but-3-en-1-yl acetate (225)



According to a procedure of Nefedov,[155] 7.48 g potassium acetate (76.2 mmol, 5.6 eq), 3.55 g 2-(1-bromobut-3-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (13.6 mmol, 1.0 eq) and 324 mg dibenzo-18-crown-6 (0.90 mmol, 0.06 eq) were dissolved in 45 mL acetonitrile and stirred overnight at 90 °C. When full conversion of the starting material was detected by GC/MS analysis the reaction mixture was quenched with H_2O and the aqueous layer was extracted three times with Et_2O, the organic layer was washed with brine, dried over $MgSO_4$, filtered and the solvent was evaporated. The crude product was purified by FC (EtOAc *n*-pentane/triethylamine 1:3:0.5) to give 1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)but-3-en-1-yl acetate (**225**) in 40% yield (1.37 g, 5.48 mmol) as colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ 5.92 – 5.77 (m, 1H, CH_{olef}), 5.15 – 5.02 (m, 2H, C$H_{2,\ olef}$), 4.02 (t, *J* = 6.8 Hz, 1H, C*H*), 2.49 – 2.41 (m, 2H, CH_2), 2.07 (s, 3H, C$H_{3,\ Ac}$), 1.25 (d, *J* = 5.8 Hz, 12H, C$H_{3,\ pin}$).

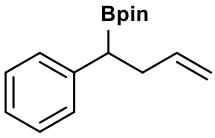
^{13}C NMR (75 MHz, $CDCl_3$) δ 173.1 (*C*=O), 135.0 (*C*H$_{olef}$), 117.1 (*C*H$_{2,\ olef}$), 83.9 ($C_{q,\ pin}$), 75.2 (*C*H), 34.9 (*C*H$_2$), 24.8 (*C*H$_{3,\ pin}$), 20.5 (*C*H$_{3,\ Ac}$).

^{11}B NMR (96 MHz, $CDCl_3$) δ 30.1 (*B*pin).

IR (neat) 2978, 2932, 1724, 1642, 1371, 1343.6, 1232, 1143, 1112, 1026, 976, 966, 915, 851, 670, 619.

HRMS (EI) calculated for $C_{11}H_{18}BO_4$: *m*/*z* = 225.1298; found *m*/*z* = 225.1282.

4,4,5,5-Tetramethyl-2-(1-phenylbut-3-en-1-yl)-1,3,2-dioxaborolane (226)



The title compound was prepared according to GP 5. First, 1.89 g (1-bromobut-3-en-1-yl)benzene (9.00 mmol, 1.0 eq) were added to a suspension of 263 mg magnesium turnings (10.8 mmol, 1.2 eq), 1.15 g pinacolborane (9.00 mmol, 1.0 eq) and 1.25 mL triethylamine (9.0 mmol, 1.0 eq) in 27 mL THF at ambient temperature. The mixture was stirred overnight at 65 °C. Then, 0.1 M HCl was added and the solution was extracted three times with diethylether, washed with brine, dried over $MgSO_4$, filtered and concentrated by rotary evaporation. The crude product was purified by FC (*n*-pentane/Et_2O 20:1) to give 4,4,5,5-tetramethyl-2-(1-phenylbut-3-en-1-yl)-1,3,2-dioxaborolane (**226**) in 52% yield (1.197 g, 4.64 mmol) as colorless liquid.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.28 – 7.20 (m, 4H, CH_{ar}), 7.16 – 7.10 (m, 1H, CH_{ar}), 5.89 – 5.76 (dddd, *J* = 17.0, 10.8, 6.8, 6.3 Hz, 1H, CH_{olef}), 5.06 – 4.91 (m, 2H, C$H_{2,\ olef}$), 2.66 – 2.55 (m, 1H, C*H*), 2.45 – 2.36 (m, 2H, CH_2), 1.20 (s, 6H, C$H_{3,\ pin}$), 1.18 (s, 6 H, C$H_{3,\ pin}$).

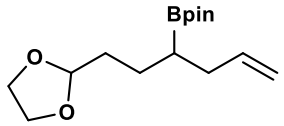
^{13}C NMR (75 MHz, $CDCl_3$) δ 142.8 ($C_{q,\ ar}$), 138.3 (*C*H$_{olef}$), 128.5 (*C*H$_{ar}$), 128.4 (*C*H$_{ar}$), 125.4 (*C*H$_{ar}$), 115.2 (*C*H$_{2,\ olef}$), 83.5 ($C_{q,\ pin}$), 36.8 (*C*H$_2$), 24.8 (*C*H$_{3,\ pin}$), 24.7 (*C*H$_{3,\ pin}$). B*C*H not detectable.

^{11}B NMR (96 MHz, $CDCl_3$) δ 33.8 (*B*pin).

IR (neat) 2978, 2928, 1359, 1323, 1245, 1141, 967, 910, 847, 763, 699, 513.

HRMS (EI) calculated for $C_{16}H_{23}BO_2$: *m*/*z* = 258.1791; found *m*/*z* = 258.1804.

2-(1-(1,3-Dioxolan-2-yl)hex-5-en-3-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (255)



The title compound was prepared according to GP 5. First, 1.80 g 2-(3-bromohex-5-en-1-yl)-1,3-dioxolane (7.67 mmol, 0.86 eq) were added to a suspension of 217 mg magnesium turnings (8.92 mmol, 1.0 eq), 1.14 g pinacolborane (8.92 mmol, 1.0 eq) and 1.24 mL triethylamine (8.92 mmol, 1.0 eq) in 30 mL anhydrous THF at ambient temperature. The mixture was stirred overnight at 80 °C. 0.1 M HCl was added and the aqueous layer was extracted three times with Et_2O. The combined organic layers were washed with brine, dried over $MgSO_4$, filtered and concentrated by rotary evaporation. The crude product was purified by FC (*n*-pentane/Et_2O 10:1) to give 2-(1-(1,3-dioxolan-2-yl)hex-5-en-3-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**255**) in 24% yield (613 mg, 2.17 mmol) as colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ 5.80 (ddt, *J* = 17.0, 10.1, 6.9 Hz, 1H, C*H*$_{olef}$), 5.05 – 4.90 (m, 2H, C*H*$_{2, olef}$), 4.83 (t, *J* = 4.8 Hz, 1H, C*H*), 3.99 – 3.79 (m, 4H, C*H*$_{2, oxolane}$), 2.26 – 2.07 (m, 2H, C*H*$_2$), 1.72–1.46 (m, 4H, C*H*$_2$), 1.22 (s, 12H, C*H*$_{3, pin}$), 1.16 – 1.05 (m, 1H, C*H*).

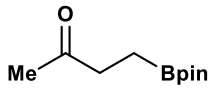
^{13}C NMR (75 MHz, $CDCl_3$) δ 138.5 (*C*H$_{olef}$), 115.1 (*C*H$_{2, olef}$), 105.0 (*C*H), 83.2 (*C*$_{q, pin}$), 65.0 (*C*H$_{2, oxolane}$), 64.9 (*C*H$_{2, oxolane}$), 35.6 (*C*H$_2$), 33.5 (*C*H$_2$), 25.3 (*C*H$_2$), 25.0 (*C*H$_{3, pin}$), 24.97 (*C*H$_{3, pin}$). B*C*H not detectable.

^{11}B NMR (96 MHz, $CDCl_3$) δ 33.8 (*B*pin).

IR (neat) 2923, 2854, 1640, 1457, 1380, 1358, 1318, 1242, 1214, 1143, 1033, 992, 968, 942, 939, 853, 836, 734, 694, 671, 647, 579, 529, 443, 395.

HRMS (ESI) calculated for $C_{15}H_{27}BO_4Li^+$: *m*/*z* = 289.1270; found *m*/*z* = 289.1281.

4-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)butan-2-one (291)



According to a procedure of Molander,[156] 12 mg CuCl (0.12 mmol, 3.0 mol%), 49 mg 1,3-bis(diphenylphosphino)propane (0.120 mmol, 3.0 mol%) and 29 mg lithium *tert*-butoxide (0.39 mmol, 10 mol%) were suspended in 4 mL anhydrous THF and stirred for 30 min at ambient temperature. 1.07 g bis(pinacolato)diboron (4.10 mmol, 1.1 eq) were dissolved in 7 mL anhydrous THF and added to the reaction mixture. After 15 min 0.34 mL methylvinylketone (4.00 mmol, 1.0 eq) as well as 0.32 mL methanol (8.00 mmol, 2.0 eq) were added and the reaction mixture was stirred overnight. H_2O was then added and the aqueous layer was extracted three times with Et_2O, the combined organic layers were dried over $MgSO_4$, filtered and the solvent was evaporated. The crude product was

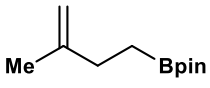
purified by FC (*n*-pentane/Et_2O 10:1) to give 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)butan-2-one (**291**) in 65% yield (516 mg, 2.60 mmol) as colorless liquid.

^{1}H NMR (300 MHz, $CDCl_3$) δ 2.58 (t, *J* = 7.1 Hz, 2H, CH_2), 2.12 (s, 3H, CH_3), 1.23 (s, 12H, C$H_{3,\,pin}$), 0.90 (t, *J* = 7.1 Hz, 2H, CH_2).

^{13}C NMR (75 MHz, $CDCl_3$) δ 209.3 (*C*=O), 83.3 ($C_{q,\,pin}$), 38.6 (*C*H_2), 29.5 (*C*H_3), 25.2 (*C*H_2), 24.9 (*C*$H_{3,\,pin}$).

The NMR spectroscopic data are in accordance with the literature.[157]

4,4,5,5-Tetramethyl-2-(3-methylbut-3-en-1-yl)-1,3,2-dioxaborolane (292)



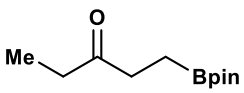
The title compound was prepared according to GP 6. First, 2.17 g methyltriphenylphosphonium bromide (6.06 mmol, 1.1 eq) and 680 mg potassium *tert*-butoxide (6.06 mmol, 1.1 eq) were suspended in 30 mL Et_2O at 0 °C. After stirring for 1 h at ambient temperature, 1.14 g 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)butan-2-one (5.77 mmol, 1.0 eq) were added dropwise and the mixture was stirred overnight. Sat. aqueous NH_4Cl solution was added and the aqueous layer was extracted three times with Et_2O. The combined organic layers were dried over $MgSO_4$, filtered, adsorbed on silica gel and the solvent was evaporated. The adsorbed crude product was purified by FC (*n*-pentane/Et_2O 8:1) to give 4,4,5,5-tetramethyl-2-(3-methylbut-3-en-1-yl)-1,3,2-dioxaborolane (**292**) in 61% yield (693 mg, 3.53 mmol) as colorless liquid.

^{1}H NMR (300 MHz, $CDCl_3$) δ 4.66 – 4.67 (m, 2H, C$H_{2,\,olef}$), 2.12 (t, *J* = 8.0 Hz, 2H, CH_2), 1.72 (s, 3H, CH_3), 1.24 (s, 12H, C$H_{3,\,pin}$), 0.93 (t, *J* = 8.1 Hz, 2H, CH_2).

^{13}C NMR (75 MHz, $CDCl_3$) δ 148.0 ($C_{q,\,olef}$), 108.6 (*C*$H_{2,\,olef}$), 83.1 ($C_{q,\,pin}$), 31.9 (*C*H_2), 25.0 (*C*$H_{3,\,pin}$), 22.6 (*C*H_3). B*C*H_2 not detectable.

The NMR spectroscopic data are in accordance with the literature.[158]

1-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)pentan-3-one (230)



According to a procedure of Molander,[156] 24 mg CuCl (0.24 mmol, 3.0 mol%), 99 mg 1,3-bis(diphenylphosphino)propane (0.37 mmol, 3.0 mol%) and 57 mg lithium *tert*-butoxide (720 mmol, 10 mol%) were suspended in 7 mL anhydrous THF and stirred for 30 min at ambient temperature. 2.13 g bis(pinacolato)diboron (8.19 mmol, 1.1 eq) were dissolved in 14 mL anhydrous THF and added to the reaction mixture.

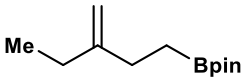
After 15 min 0.80 mL ethylvinylketone (8.00 mmol, 1.0 eq) as well as 0.64 mL methanol (16.0 mmol, 2.0 eq) were added and the reaction mixture was stirred overnight. H_2O was then added, and the aqueous layer was extracted three times with Et_2O, the combined organic layer was dried over $MgSO_4$, filtered and the solvent was evaporated. The crude product was purified by FC (*n*-pentane/Et_2O 8:1) to give 1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pentan-3-one (**230**) in 90% yield (1.52 g, 7.17 mmol) as colorless liquid.

^{1}H NMR (300 MHz, $CDCl_3$) δ 2.55 (t, *J* = 7.1 Hz, 2H, C*H*$_2$), 2.40 (q, *J* = 7.5 Hz, 2H, C*H*$_2$), 1.23 (s, 12H, C*H*$_{3,\ pin}$), 1.05 (t, *J* = 7.4 Hz, 3H, C*H*$_3$), 0.91 (t, *J* = 7.1 Hz, 2H, C*H*$_2$).

^{13}C NMR (75 MHz, $CDCl_3$) δ 212.0 (*C*=O), 83.2 (*C*$_{q,\ pin}$), 37.1 (*C*H$_2$), 35.5 (*C*H$_2$), 24.9 (*C*H$_{3,\ pin}$), 8.2 (*C*H$_3$). B*C*H$_2$ not detectable.

The NMR spectroscopic data are in accordance with the literature.[159]

4,4,5,5-Tetramethyl-2-(3-methylenepentyl)-1,3,2-dioxaborolane (231)



The title compound was prepared according to GP 6. First, 4.59 g methyltriphenylphosphonium bromide (12.9 mmol, 1.1 eq) and 1.45 g potassium *tert*-butoxide (12.9 mmol, 1.1 eq) were suspended in 65 mL THF at 0 °C. After stirring for 1 h at ambient temperature, 2.61 g 1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pentan-3-one (12.3 mmol, 1.0 eq) were added dropwise and the mixture was stirred overnight. Sat. aqueous NH_4Cl solution was added and the aqueous layer was extracted three times with Et_2O. The combined organic layers were dried over $MgSO_4$, filtered, adsorbed on silica gel and the solvent was evaporated. The adsorbed crude product was purified by FC (*n*-pentane/Et_2O 8:1) to give 4,4,5,5-tetramethyl-2-(3-methylenepentyl)-1,3,2-dioxaborolane (**231**) in 67% yield (1.73 g, 8.23 mmol) as colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ 4.69 (d, *J* = 9.1 Hz, 2H, C*H*$_{2,\ olef}$), 2.14 (t, *J* = 8.0 Hz, 2H, C*H*$_2$), 2.03 (q, *J* = 7.4 Hz, 2H, C*H*$_2$), 1.24 (s, 12H, C*H*$_{3,\ pin}$), 1.02 (t, *J* = 7.5 Hz, 3H, C*H*$_3$), 0.93 (t, *J* = 8.0 Hz, 2H, C*H*$_2$).

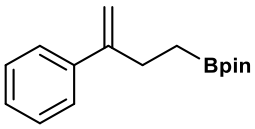
^{13}C NMR (75 MHz, $CDCl_3$) δ 106.5 (*C*H$_{2,\ olef}$), 83.1 (*C*$_{q,\ pin}$), 30.3 (*C*H$_2$), 29.0 (*C*H$_2$), 25.0 (*C*H$_{3,\ pin}$), 12.6 (*C*H$_3$). B–*C*H$_2$ not visible.

^{11}B NMR (96 MHz, $CDCl_3$) δ 33.8 (*B*pin).

IR (neat) 2978, 2933, 1646, 1370, 1316, 1144, 968, 884, 869, 796.

HRMS (EI) calculated for $C_{12}H_{23}BO_2$: *m*/*z* = 210.1791; found *m*/*z* = 210.1786.

4,4,5,5-Tetramethyl-2-(3-phenylbut-3-en-1-yl)-1,3,2-dioxaborolane (232)



The title compound was prepared according to GP 6. First, 740 mg methyltriphenylphosphonium bromide (2.10 mmol, 1.1 eq) and 230 mg potassium *tert*-butoxide (2.10 mmol, 1.1 eq) were suspended in 12 mL Et_2O at 0 °C. After stirring for 50 min at ambient temperature, 500 mg 1-phenyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)propan-1-one (1.90 mmol, 1.0 eq) were added dropwise and the mixture was stirred overnight. NH_4Cl solution was added and the aqueous layer was extracted three times with Et_2O, dried over $MgSO_4$, filtered, adsorbed on silica gel and the solvent was evaporated. The adsorbed crude product was purified by FC (*n*-pentane/Et_2O 10:1) to give 4,4,5,5-tetramethyl-2-(3-phenylbut-3-en-1-yl)-1,3,2-dioxaborolane (**232**) in 31% yield (150 mg, 0.580 mmol) as pale yellow oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.42 – 7.24 (m, 5H, CH_{ar}), 5.23 (s, 1H, CH_{olef}), 5.07 (s, 1H, H CH_{olef}), 2.61 (t, *J* = 7.80 Hz, 2H, CH_2), 1.24 (s, 12H, C$H_{3,\ pin}$), 0.99 (t, *J* = 8.10 Hz, 2H, CH_2).

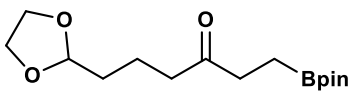
^{13}C NMR (75 MHz, $CDCl_3$) δ 150.6 ($C_{q,\ olef}$), 142.0 ($C_{q,\ ar}$), 128.3 (CH_{ar}), 127.3 (CH_{ar}), 126.4 (CH_{ar}), 111.2 ($CH_{2,\ olef}$), 83.2 ($C_{q,\ pin}$), 29.6 (CH_2), 25.0 ($CH_{3,\ pin}$). BCH_2 not detectable.

^{11}B NMR (96 MHz, $CDCl_3$) δ 34.2 (*B*pin).

IR (neat) 3081, 3056, 2977, 2292, 1627, 1600, 1574, 1494, 1443, 1403, 1369, 1318, 1244, 1213, 1164, 1142, 1109, 1072, 1004, 967, 888, 869, 846, 776, 700, 673, 577, 541, 513, 388.

HRMS (EI) calculated for $C_{16}H_{23}BO_2$: *m*/*z* = 258.1791; found *m*/*z* = 258.1782.

6-(1,3-Dioxolan-2-yl)-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hexan-3-one (293)



According to a procedure of Molander,[156] 37 mg CuCl (0.37 mmol, 3.0 mol%), 154 mg 1,3-bis(diphenylphosphino)propane (0.37 mmol, 3.0 mol%) and lithium *tert*-butoxide (99.6 mg, 1.2 mmol, 10 mol%) were suspended in 12 mL anhydrous Et_2O and stirred for 30 min at ambient temperature. Then, 3.32 g bis(pinacolato)diboron (13.1 mmol, 1.1 eq) were dissolved in 12 mL anhydrous Et_2O and added to the reaction mixture. After 15 min 2.12 g 6-(1,3-dioxolan-2-yl)hex-1-en-3-one (12.4 mmol, 1.0 eq) as well as 1.0 mL methanol (24.7 mmol, 2.0 eq) were added and the reaction mixture was stirred overnight. H_2O was then added and the aqueous layer was extracted three times with Et_2O, the combined organic layer was dried over $MgSO_4$, filtered and the solvent was evaporated. The crude product was purified by FC

(*n*-pentane/Et_2O 1:1) to give 6-(1,3-dioxolan-2-yl)-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hexan-3-one (**293**) in 92% yield (3.41 g, 11.5 mmol) as colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ 4.84 (t, *J* = 4.3 Hz, 1H, C*H*), 3.98 – 3.82 (m, 4H, C$H_{2,\ oxolane}$), 2.55 (t, *J* = 7.1 Hz, 2H, CH_2), 2.45 (t, *J* = 7.0 Hz, 2H, CH_2), 1.77 – 1.59 (m, 4H, CH_2), 1.29 – 1.21 (m, 12H, C$H_{3,\ pin}$), 0.90 (t, *J* = 7.1 Hz, 2H, CH_2).

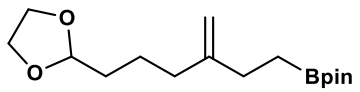
^{13}C NMR (75 MHz, $CDCl_3$) δ 211.1 (*C*=O), 104.5 (*C*H), 83.2 ($C_{q,\ pin}$), 65.0 (*C*$H_{2,\ oxolane}$), 42.0 (*C*H_2), 37.6 (*C*H_2), 33.3 (*C*H_2), 24.9 (*C*$H_{3,\ pin}$), 18.6 (*C*H_2). B*C*H_2 not detectable.

^{11}B NMR (96 MHz, $CDCl_3$) δ 33.1 (*B*pin).

IR (neat) 2977, 2887, 1711, 1473, 1453, 1418, 1371, 1313, 1142, 1036, 1009, 983, 967, 949, 875, 850, 699, 673.

HRMS (EI) calculated for $C_{15}H_{27}BO_5$: *m*/*z* = 298.1952; found *m*/*z* = 298.1943.

2-(6-(1,3-Dioxolan-2-yl)-3-methylenehexyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (259)



The title compound was prepared according to GP 6. 6.67 g methyltriphenylphosphonium bromide (18.7 mmol, 1.5 eq) and 2.23 g potassium *tert*-butoxide (19.9 mmol, 1.6 eq) were suspended in 60 mL Et_2O at 0 °C. After stirring for 45 min at ambient temperature, 3.71 g 6-(1,3-dioxolan-2-yl)-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hexan-3-one (12.4 mmol, 1.0 eq) were added dropwise and the mixture was stirred overnight. Sat. aqueous NH_4Cl solution was added and the aqueous layer was extracted three times with Et_2O, dried over $MgSO_4$, filtered, adsorbed on silica gel and the solvent was evaporated. The adsorbed crude product was purified by FC (*n*-pentane/Et_2O 3:1) to give 2-(6-(1,3-dioxolan-2-yl)-3-methylenehexyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**259**) in 30% yield (1.11 g, 3.75 mmol) as colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ 4.86 (t, *J* = 4.6 Hz, 1H, C*H*), 4.73 (d, *J* = 1.4 Hz, 1H, CH_{olef}), 4.69 (d, *J* = 0.8 Hz, 1H, CH_{olef}), 3.99 – 3.81 (m, 4H, C$H_{2,\ oxolane}$), 2.17 – 2.02 (m, 4H, CH_2), 1.70 – 1.49 (m, 4H, CH_2), 1.23 (s, 12H, C$H_{3,\ pin}$), 0.96 – 0.88 (m, 2H, CH_2).

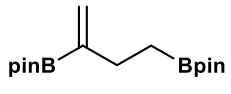
^{13}C NMR (75 MHz, $CDCl_3$) δ 151.3 ($C_{q,\ olef}$), 108.1 (*C*$H_{2,\ olef}$), 104.8 (*C*H_2), 83.1 ($C_{q,\ pin}$), 65.0 (*C*$H_{2,\ oxolane}$), 36.2 (*C*H_2), 33.8 (*C*H_2), 30.0 (*C*H_2), 25.0 (*C*$H_{2,\ pin}$), 22.4 (*C*H_2). B*C*H_2 not detectable.

^{11}B NMR (96 MHz, $CDCl_3$) δ 33.9 (*B*pin).

IR (neat) 2935, 2882, 1645, 1434, 1405, 1370, 1317, 1273, 1238, 1214, 1143, 1034, 968, 943, 885, 847, 753, 708, 673, 578, 541, 440, 380.

HRMS (EI) calculated for $C_{15}H_{26}BO_4$: *m*/*z* = 281.1924; found *m*/*z* = 281.1934.

2,2'-(But-3-ene-1,3-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (229)



The title compound was prepared according to GP 5. 175 mg magnesium turnings (7.20 mmol, 1.2 eq), 768 mg pinacolborane (6.00 mmol, 1.0 eq) and 0.83 mL NEt_3 (6.00 mmol, 1.0 eq) were suspended in 20 mL THF. 1.57 g 2-(3-bromobut-3-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (6.00 mmol, 1.0 eq) were added at ambient temperature and the reaction mixture was stirred overnight at 75 °C. The reaction was quenched with 0.1 M aqueous HCl, the aqueous layer was extracted three times with Et_2O, the aqueous layer was washed with brine, dried over $MgSO_4$ and filtered. The solvent was removed under reduced pressure and the crude product was purified by FC (*n*-pentane) to give 2,2'-(but-3-ene-1,3-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (**229**) in 41% yield (760 mg, 2.47 mmol) as colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ 5.72 (d, *J* = 2.3 Hz, 1H, C*H*$_{olef}$), 5.61 (s, 1H, C*H*$_{olef}$), 2.26 (t, *J* = 8.1 Hz, 2H, C*H*$_2$), 1.25 (s, 12H, C*H*$_{3, pin}$), 1.23 (s, 12H, C*H*$_{3, pin}$), 0.92 (t, *J* = 8.1 Hz, 2H, C*H*$_2$).

^{13}C NMR (75 MHz, $CDCl_3$) δ 127.7 (*C*H$_{2, olef}$), 83.4 (*C*$_{q, pin}$), 83.0 (*C*$_{q, pin}$), 29.3 (*C*H$_2$), 25.0 (*C*H$_{3, pin}$), 24.9 (*C*H$_{3, pin}$). B*C*H$_2$ not detectable.

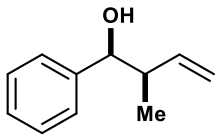
^{11}B NMR (96 MHz, $CDCl_3$) δ 33.7 (*B*pin), 30.0 (*B*pin).

IR (neat) 2977, 2930, 1447, 1369, 1309, 1214, 1190, 967, 864, 848, 672, 578.

HRMS (EI) calculated for $C_{16}H_{30}B_2O_4$: *m*/*z* = 308.2330; found *m*/*z* = 308.2340.

5.5.2 Isomerization/Allylboration Sequence

***syn*-2-Methyl-1-phenylbut-3-en-1-ol (112)**



The title compound was prepared according to GP 7 utilizing 27 mg Ni(dppp)Cl_2 (50 µmol, 10 mol%), 6.6 mg zinc powder and 32 mg zinc iodide (100 µmol, 20 mol% each). These materials were suspended in 0.3 mL dichloromethane and 0.2 mL of the $HPPh_2$ solution (0.125 M in dichloromethane, 25 µmol, 5.0 mol%) were added. After cooling to −50 °C, 53 mg benzaldehyde and 91 mg 2-(but-3-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (0.50 mmol, 1.0 eq each) were added. The

reaction mixture was stirred for 7 h at −50 °C. After general workup and purification by FC (*n*-pentane/Et_2O 10:1) 2-methyl-1-phenylbut-3-en-1-ol (**112**) was obtained as *syn*/*anti* mixture (98:2) in 81% yield (66 mg, 0.407 mmol) as colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.37 – 7.24 (m, 5H, CH_{ar}), 5.82 – 5.71 (m, 1H, CH_{olef}), 5.09 – 5.03 (m, 2H, C$H_{2,\ olef}$), 4.62 (dd, *J* = 5.2 Hz, 3.1 Hz, 1H, C*H*), 2.65 – 2.54 (m, 1H, C*H*), 1.95 (d, *J* = 2.9 Hz, O*H*), 1.02 (d, *J* = 7.0 Hz, 3H, CH_3).

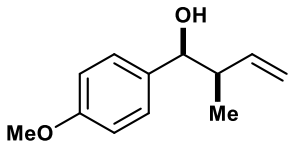
^{13}C NMR (75 MHz, $CDCl_3$) δ 142.8 ($C_{q,\ ar}$), 140.5 (CH_{olef}), 128.2 (*C*H_{ar}), 127.5 (*C*H_{ar}), 126.7 (*C*H_{ar}), 115.7 (*C*$H_{2,\ olef}$), 77.5 (*C*H), 44.8 (*C*H), 14.2 (*C*H_3).

Resolved signals of the minor diastereomer *anti*-2-methyl-1-phenylbut-3-en-1-ol:

^{1}H NMR (300 MHz, $CDCl_3$) δ 4.37 (dd, *J* = 7.9 Hz, 2.2 Hz, 1H, C*H*), 2.15 (d, *J* = 1.9 Hz, 1H, O*H*), 0.88 (d, *J* = 7.0 Hz, 3H, CH_3).

The NMR spectroscopic data for both diastereomers are in accordance with the literature.[160,161]

***syn*-(4-Methoxyphenyl)-2-methylbut-3-en-1-ol (233a)**



The title compound was prepared according to GP 7 utilizing 27 mg Ni(dppp)Cl_2 (50 μmol, 10 mol%), 6.6 mg zinc powder and 32 mg zinc iodide (100 μmol, 20 mol% each). These materials were suspended in 0.3 mL dichloromethane and 0.2 mL of the $HPPh_2$ solution (0.125 M in dichloromethane, 25 μmol, 5.0 mol%) were added. After cooling to −50 °C, 68 mg 4-methoxybenzaldehyde and 89 mg 2-(but-3-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (0.50 mmol, 1.0 eq each) were added. The reaction mixture was stirred for 5 h at −50 °C. After general workup and purification by FC (*n*-pentane/Et_2O 12:1→8:1) (4-methoxyphenyl)-2-methylbut-3-en-1-ol (**233a**) was obtained as *syn*/*anti* mixture (96:4) in 81% yield (78 mg, 0.406 mmol) as colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.22 (ddd, *J* = 8.6, 2.7, 1.9 Hz, 2H, CH_{ar}), 6.87 (ddd, *J* = 8.7, 2.8, 2.0 Hz, 2H, CH_{ar}), 5.79 – 5.68 (m, 1H, CH_{olef}), 5.07 – 5.00 (m, 2H, C$H_{2,\ olef}$), 4.55 (dd, *J* = 5.8, 2.6 Hz, 1H, C*H*), 3.80 (s, 3H, OCH_3), 2.61 – 2.51 (m, 1H, C*H*), 1.86 (d, *J* = 3.0 Hz, 1H, O*H*), 1.02 (d, *J* = 6.8 Hz, 3H, CH_3).

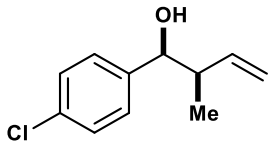
^{13}C NMR (75 MHz, $CDCl_3$) δ 159.1 ($C_{q,\ ar}$), 140.5 (*C*H_{olef}), 135.0 ($C_{q,\ ar}$), 127.8 (*C*H_{ar}), 115.5 (*C*$H_{2,\ olef}$), 113.7 (*C*H_{ar}), 77.2 (*C*H), 55.4 (O*C*H_3), 44.8 (*C*H), 14.5 (*C*H_3).

Resolved signals of the minor diastereomer *anti*-(4-methoxyphenyl)-2-methylbut-3-en-1-ol:

^{1}H NMR (300 MHz, $CDCl_3$) δ 5.85 (dd, *J* = 17.4, 10.2 Hz, 1H, C*H*$_{olef}$), 5.23 – 5.16 (m, 2H, C*H*$_{2,\ olef}$), 4.30 (d, *J* = 7.4 Hz, 1H, C*H*), 2.49 – 2.42 (m, 1H, C*H*), 2.09 (s, 1H, O*H*), 0.85 (d, *J* = 6.9 Hz, 3H, C*H*$_3$).

The NMR spectroscopic data for both diastereomers are in accordance with the literature.[160–162]

syn-1-(4-Chlorophenyl)-2-methylbut-3-en-1-ol (233b)



The title compound was prepared according to GP 7 utilizing 14 mg Ni(dppp)Cl_2 (25 μmol, 10 mol%), 3.3 mg zinc powder and 16 mg zinc iodide (50 μmol, 20 mol% each). These materials were suspended in 0.15 mL dichloromethane and stirred for 10 min. Then, 0.1 mL of the $HPPh_2$ solution (0.125 M in dichloromethane, 12.5 μmol, 5.0 mol%) were added. After cooling to –40 °C, 35 mg 4-chlorobenzaldehyde and 45 mg 2-(but-3-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (0.25 mmol, 1.0 eq each) were added. The reaction mixture was stirred for 1 h at –40 °C. After general workup and purification by FC (*n*-pentane/Et_2O 10:1) 1-(4-chlorophenyl)-2-methylbut-3-en-1-ol (**233b**) was obtained as *syn*/*anti* mixture (97:3) in 98% yield (48 mg, 0.244 mmol) as colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.33 – 7.21 (m, 4H, C*H*$_{ar}$), 5.80 – 5.68 (m, 1H, C*H*$_{olef}$), 5.10 – 5.02 (m, 2H, C*H*$_{2,\ olef}$), 4.61 (d, *J* = 5.3 Hz, 1H, C*H*), 2.60 – 2.49 (m, 1H, C*H*), 1.93 (s, 1H, O*H*), 0.98 (d, *J* = 6.7 Hz, 3H, C*H*$_3$).

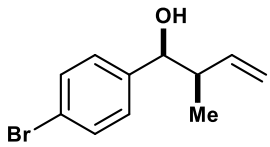
^{13}C NMR (75 MHz, $CDCl_3$) δ 141.1 (*C*$_{q,\ ar}$), 140.1 (*C*H$_{olef}$), 133.2 (*C*$_{q,\ ar}$), 128.4 (*C*H$_{ar}$), 128.0 (*C*H$_{ar}$), 116.1 (*C*H$_{2,\ olef}$), 76.7 (*C*H), 44.8 (*C*H), 14.0 (*C*H$_3$).

Resolved signals of the minor diastereomer *anti*-1-(4-chlorophenyl)-2-methylbut-3-en-1-ol:

^{1}H NMR (300 MHz, $CDCl_3$) δ 4.85 – 4.79 (m, 2H, C*H*$_{2,\ olef}$), 4.35 (d, *J* = 7.7 Hz, 1H, C*H*), 2.42 – 1.93 (m, 1H, C*H*), 0.88 (d, *J* = 6.9 Hz, 3H, C*H*$_3$).

The NMR spectroscopic data for both diastereomers are in accordance with the literature.[163]

syn-1-(4-Bromophenyl)-2-methylbut-3-en-1-ol (233c)



The title compound was prepared according to GP 7 utilizing 27 mg Ni(dppp)Cl_2 (50 μmol, 10 mol%), 6.6 mg zinc powder and 32 mg zinc iodide (100 μmol, 20 mol% each). These materials were suspended in

0.3 mL dichloromethane and 0.2 mL of the $HPPh_2$ solution (0.125 M in dichloromethane, 25 μmol, 5.0 mol%) were added. After cooling to −50 °C, 92 mg 4-bromobenzaldehyde and 91 mg 2-(but-3-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (0.5 mmol, 1.0 eq each) were added. The reaction mixture was stirred for 5 h and 30 min at −50 °C. After general workup and purification by FC (*n*-pentane/Et_2O 12:1) 1-(4-bromophenyl)-2-methylbut-3-en-1-ol (**233c**) was obtained as *syn*/*anti* mixture (97:3) in 77% yield (93 mg, 0.386 mmol) as colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.46 (ddd, *J* = 8.4, 2.4, 1.9 Hz, 2H, CH_{ar}), 7.18 (ddd, *J* = 8.3, 2.2, 1.6 Hz, 2H, CH_{ar}), 5.80 – 5.69 (m, 1H, CH_{olef}), 5.10 – 5.02 (m, 2H, C$H_{2,\ olef}$), 4.59 (d, *J* = 5.3 Hz, 1H, C*H*), 2.61 – 2.49 (m, 1H, C*H*), 1.92 (s, 1H, O*H*), 0.98 (d, *J* = 6.9 Hz, 3H, CH_3).

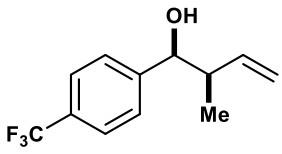
^{13}C NMR (75 MHz, $CDCl_3$) δ 140.0 (*C*H_{olef}), 131.3 (*C*H_{ar}), 128.4 (*C*H_{ar}), 121.3 (*C*$_{q,\ ar}$), 116.1 (*C*$H_{2,\ olef}$), 76.7 (*C*H), 44.7 (*C*H), 13.9 (*C*H_3). Br*C*$_{q,\ ar}$ not detectable.

Resolved signals of the minor diastereomer *anti*-1-(4-bromophenyl)-2-methylbut-3-en-1-ol:

^{1}H NMR (300 MHz, $CDCl_3$) δ 5.22 – 5.16 (m, 2H, C$H_{2,\ olef}$), 4.34 (d, *J* = 7.7 Hz, 1H, C*H*), 2.47 – 2.39 (m, 1H, C*H*), 0.88 (d, *J* = 6.9 Hz, 3H, CH_3).

The NMR spectroscopic data for both diastereomers are in accordance with the literature.[164]

***syn*-2-Methyl-1-(4-(trifluoromethyl)phenyl)but-3-en-1-ol (233d)**



The title compound was prepared according to GP 7 utilizing 27 mg $Ni(dppp)Cl_2$ (50 μmol, 10 mol%), 6.6 mg zinc powder and 32 mg zinc iodide (100 μmol, 20 mol% each). These materials were suspended in 0.3 mL dichloromethane and 0.2 mL of the $HPPh_2$ solution (0.125 M in dichloromethane, 25 μmol, 5.0 mol%) were added. After cooling to −40 °C, 87 mg 4-trifluoromethylbenzaldehyde and 91 mg 2-(but-3-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (0.50 mmol, 1.0 eq each) were added. The reaction mixture was stirred for 7 h at −40 °C and overnight at ambient temperature. After general workup and purification by FC (*n*-pentane/Et_2O 10:1) 2-methyl-1-(4-(trifluoromethyl)phenyl)but-3-en-1-ol (**233d**) was obtained as *syn*/*anti* mixture (95:5) in 76% yield (88 mg, 0.382 mmol) as colorless oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.59 (d, *J* = 8.1 Hz, 2H, CH_{ar}), 7.43 (d, *J* = 8.1 Hz, 2H, CH_{ar}), 5.83 – 5.72 (m, 1H, CH_{olef}), 5.13 – 5.05 (m, 2H, C$H_{2,\ olef}$), 4.71 (d, *J* = 5.1 Hz, 1H, C*H*), 2.65 – 2.54 (m, 1H, C*H*), 1.98 (s, 1H, O*H*), 0.99 (d, *J* = 6.9 Hz, 3H, CH_3).

^{13}C NMR (125 MHz, $CDCl_3$) δ 146.6 ($C_{q, ar}$), 139.8 (CH_{olef}), 129.6 (q, J = 32.3 Hz, $CF_3C_{q, ar}$), 126.9 (CH_{ar}), 125.1 (q, J = 3.8 Hz, CH_{ar}), 116.4 ($CH_{2, olef}$), 76.6 (*C*H), 44.7 (*C*H), 13.6 (CH_3). CF_3 not detectable.

^{19}F NMR (282 MHz, $CDCl_3$) δ –62.55 (s, CF_3).

Resolved signals of the minor diastereomer *anti*-2-methyl-1-(4-(trifluoromethyl)phenyl)but-3-en-1-ol:

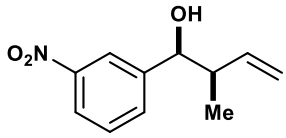
^{1}H NMR (500 MHz, $CDCl_3$) δ 5.23 – 5.17 (m, 2H, $CH_{2, olef}$), 4.45 (d, J = 7.6 Hz, 1H. C*H*), 2.51 – 2.44 (m, 1H, C*H*), 0.91 (d, J = 7.0 Hz, 3H, CH_3).

^{13}C NMR (125 MHz, $CDCl_3$) δ 139.9 (CH_{olef}), 125.3 (q, J = 3.7 Hz, CH_{ar}), 117.8 ($CH_{2, olef}$), 77.3 (*C*H), 46.5 (*C*H), 16.5 (CH_3).

^{19}F NMR (282 MHz, $CDCl_3$) δ –62.59 (s, CF_3).

The NMR spectroscopic data for the *syn*-configured diastereomer are in accordance with the literature.[165]

syn-2-Methyl-1-(3-nitrophenyl)but-3-en-1-ol (233e)



The title compound was prepared according to GP 7 utilizing 27 mg $Ni(dppp)Cl_2$ (50 μmol, 10 mol%), 6.6 mg zinc powder and 32 mg zinc iodide (100 μmol, 20 mol% each). These materials were suspended in 0.3 mL dichloromethane and 0.2 mL of the $HPPh_2$ solution (0.125 M in dichloromethane, 25 μmol, 5.0 mol%) were added. After cooling to –40 °C, 71 mg 3-nitrobenzaldehyde and 91 mg 2-(but-3-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (0.50 mmol, 1.0 eq each) were added. The reaction mixture was stirred for 7 h at –40 °C and overnight at ambient temperature. After general workup and purification by FC (*n*-pentane/Et_2O 10:1 → 8:1) 2-methyl-1-(3-nitrophenyl)but-3-en-1-ol (**233e**) was obtained as *syn*/*anti* mixture (98:2) in 61% yield (62 mg, 0.304 mmol) as colorless oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.19 (d, 1H, CH_{ar}), 8.13 – 8.11 (m, 1H, CH_{ar}), 7.65 (dd, J = 7.7, 0.5 Hz, 1H, CH_{ar}), 7.50 (t, J = 7.9 Hz, 1H, CH_{ar}), 5.82 – 5.75 (m, 1H, CH_{olef}), 5.14 – 5.07 (m, 2H, $CH_{2, olef}$), 4.77 (d, J = 5.0 Hz, 1H, C*H*), 2.65 – 2.58 (m, 1H, C*H*), 2.10 (s, 1H, O*H*), 0.99 (d, J = 6.9 Hz, 3H, CH_3).

^{13}C NMR (75 MHz, $CDCl_3$) δ 144.9 ($C_{q, ar}$), 139.5 (CH_{olef}), 132.7 (CH_{ar}), 129.1 (CH_{ar}), 122.5 (CH_{ar}), 121.6 (CH_{ar}), 116.8 ($CH_{2, olef}$), 76.2 (*C*H), 44.8 (*C*H), 13.6 (CH_3).

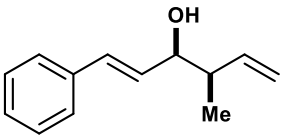
IR (neat) 3430, 3081, 2971, 2876, 1524, 1347, 1200, 1095, 1029, 999, 917, 807, 739, 690.

HRMS (EI) calculated for $C_{11}H_{13}NO_3$: *m*/*z* = 207.0895; found *m*/*z* = 207.0885.

Resolved signals of the minor diastereomer *anti*-2-methyl-1-(3-nitrophenyl)but-3-en-1-ol:

^{1}H NMR (300 MHz, $CDCl_3$) δ 5.24 – 5.19 (m, 2H, C*H*$_{2,\ olef}$), 4.50 (d, *J* = 7.6 Hz, 1H, C*H*), 2.51 – 2.46 (m, 1H, C*H*), 0.94 (d, *J* = 6.9 Hz, 3H, C*H*$_3$).

***syn*-4-Methyl-1-phenylhexa-1,5-dien-3-ol (233f)**



The title compound was prepared according to GP 7 utilizing 27 mg Ni(dppp)Cl_2 (50 μmol, 10 mol%), 6.6 mg zinc powder and 32 mg zinc iodide (100 μmol, 20 mol% each). These materials were suspended in 0.3 mL dichloromethane and 0.2 mL of the $HPPh_2$ solution (0.125 M in dichloromethane, 25 μmol, 5.0 mol%) were added. After cooling to –40 °C, 66 mg cinnamaldehyde and 91 mg 2-(but-3-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (0.50 mmol, 1.0 eq each) were added. The reaction mixture was stirred for 6 h at –40 °C. After general workup and purification by FC (*n*-pentane/Et_2O 10:1) 4-methyl-1-phenylhexa-1,5-dien-3-ol (**233f**) was obtained as *syn*/*anti* mixture (92:8) in 96% yield (90 mg, 0.478 mmol) as colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.40 – 7.22 (m, 5H, C*H*$_{ar}$), 6.60 (d, *J* = 16.0 Hz, 1H, C*H*$_{olef}$), 6.24 (dd, *J* = 15.6 Hz, 6.3 Hz, 1H, C*H*$_{olef}$), 5.91 – 5.79 (m, 1H, C*H*$_{olef}$), 5.18 – 5.12 (m, 2H, C*H*$_{2,\ olef}$), 4.22 (dd, *J* = 10.3 Hz, 5.0 Hz, 1H, C*H*), 2.54 – 2.43 (m, 1H, C*H*), 1.70 (d, *J* = 4.9 Hz, 1H, O*H*), 1.09 (d, *J* = 7.0 Hz, 3H, C*H*$_3$).

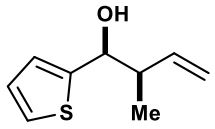
^{13}C NMR (75 MHz, $CDCl_3$) δ 140.1 (*C*H$_{olef}$), 137.0 (*C*$_{q,\ ar}$), 131.4 (*C*H$_{olef}$), 130.2 (*C*H$_{olef}$), 128.7 (*C*H$_{ar}$), 127.8 (*C*H$_{ar}$), 126.6 (*C*H$_{ar}$), 116.2 (*C*H$_{2,\ olef}$), 75.9 (*C*H), 44.1 (*C*H), 15.0 (*C*H$_3$).

Resolved signals of the minor diastereomer *anti*-4-methyl-1-phenylhexa-1,5-dien-3-ol:

^{1}H NMR (300 MHz, $CDCl_3$) δ 4.06 (m, 1H, C*H*), 2.41 – 2.34 (m, 1H, C*H*), 1.83 (d, *J* = 3.4 Hz, 1H, O*H*), 1.02 (d, *J* = 6.8 Hz, 3H, C*H*$_3$).

The NMR spectroscopic data for the *anti*-configured diastereomer are in accordance with the literature.[164,166]

***syn*-2-Methyl-1-(thiophen-2-yl)but-3-en-1-ol (233g)**



The title compound was prepared according to GP 7 utilizing 28 mg Ni(dppp)Cl_2 (50 μmol, 10 mol%), 6.6 mg zinc powder and 32 mg zinc iodide (100 μmol, 20 mol% each). These materials were suspended in 0.3 mL dichloromethane and stirred for 10 min. Then, 0.2 mL of the $HPPh_2$ solution (0.125 M in dichloromethane, 25 μmol, 5.0 mol%) were added. After cooling to –50 °C, 56 mg thiophene-2-carbaldehyde and 91 mg 2-(but-3-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (0.50 mmol, 1.0 eq each) were added. The reaction mixture was stirred for 2 h at –50 °C and overnight at ambient temperature. After general workup and purification by FC (*n*-pentane/Et_2O 10:1) 2-methyl-1-(thiophen-2-yl)but-3-en-1-ol (**233g**) was obtained as *syn*/*anti* mixture (86:14) in 56% yield (47 mg, 0.279 mmol) as pale-yellow oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.24 (dd, *J* = 4.8, 1.4 Hz, 1H, C*H*$_{ar}$), 6.98 – 6.94 (m, 2H, C*H*$_{ar}$), 5.89 – 5.74 (m, 1H, C*H*$_{olef}$), 5.14 – 5.10 (m, 1H, C*H*$_{olef}$), 5.07 (d, *J* = 1.1 Hz, 1H, C*H*$_{olef}$), 4.85 (d, *J* = 5.8 Hz, 1H, C*H*), 2.70 – 2.58 (m, 1H, C*H*), 2.07 (s, 1H, O*H*), 1.09 (d, *J* = 6.8 Hz, 3H, C*H*$_3$).

^{13}C NMR (75 MHz, $CDCl_3$) δ 146.7 (*C*H$_{ar}$), 139.8 (*C*H$_{olef}$), 126.6 (*C*H$_{ar}$), 124.6 (*C*H$_{ar}$), 124.4 (*C*H$_{ar}$), 116.2 (*C*H$_{2,\ olef}$), 74.0 (*C*H), 45.2 (*C*H), 14.9 (*C*H$_3$).

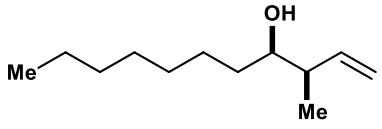
IR (neat) 3409, 3076, 2969, 2930, 2872, 1659, 1439, 1417, 1261, 1005, 914, 854, 829, 695.

HRMS (EI) calculated for $C_9H_{12}OS$: *m*/*z* = 168.0609; found *m*/*z* = 168.0605.

Resolved signals of the minor diastereomer *anti*-2-methyl-1-(thiophen-2-yl)but-3-en-1-ol:

^{1}H NMR (300 MHz, $CDCl_3$) δ 5.27 – 5.18 (m, 2H, C*H*$_{2,\ olef}$), 4.66 (d, *J* = 7.7 Hz, 1H, C*H*), 2.58 – 2.51 (m, 1H, C*H*), 2.26 (s, 1H, O*H*), 0.96 (d, *J* = 6.8 Hz, 3H, C*H*$_3$).

***syn*-3-Methylundec-1-en-4-ol (233h)**



The title compound was prepared according to GP 7 utilizing 27 mg Ni(dppp)Cl_2 (50 μmol, 10 mol%), 6.6 mg zinc powder and 32 mg zinc iodide (100 μmol, 20 mol% each). These materials were suspended in 0.3 mL dichloromethane and 0.2 mL of the $HPPh_2$ solution (0.125 M in dichloromethane, 25 μmol, 5.0 mol%) were added. After cooling to –45 °C, 65 mg octanal and 91 mg 2-(but-3-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (0.50 mmol, 1.0 eq each) were added. The reaction mixture was stirred for 5 h at –45 °C and overnight at

ambient temperature. After general workup and purification by FC (*n*-pentane/Et_2O 20:1) 3-methylundec-1-en-4-ol (**233h**) was obtained as *syn*/*anti* mixture (93:7) in 78% yield (72 mg, 0.391 mmol) as colorless liquid.

^{1}H NMR (300 MHz, $CDCl_3$) δ 5.86 – 5.74 (m, 1H, C*H*$_{olef}$), 5.13 – 5.05 (m, 2H, C*H*$_{2,\ olef}$), 3.49 (m, 1H, C*H*), 2.33 – 2.19 (m, 1H, C*H*), 1.48 (br s, 1H, O*H*), 1.28 (br s, 12H, C*H*$_2$), 1.03 (d, *J* = 6.9 Hz, 3H, C*H*$_3$), 0.88 (t, *J* = 7.0 Hz, 3H, C*H*$_3$).

^{13}C NMR (75 MHz, $CDCl_3$) δ 141.2 (*C*H$_{olef}$), 115.1 (*C*H$_{2,\ olef}$), 74.8 (*C*H), 43.4 (*C*H), 34.1 (*C*H$_2$), 31.8 (*C*H$_2$), 29.6 (*C*H$_2$), 29.3 (*C*H$_2$), 26.1 (*C*H$_2$), 22.6 (*C*H$_2$), 14.02 (*C*H$_3$), 13.99 (*C*H$_3$).

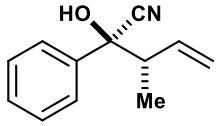
Resolved signals of the minor diastereomer *anti*-3-methylundec-1-en-4-ol:

^{1}H NMR (300 MHz, $CDCl_3$) δ 3.38 (m, 1H, C*H*), 1.04 (d, *J* = 6.9 Hz, 3H, C*H*$_3$).

^{13}C NMR (75 MHz, $CDCl_3$) δ 140.4 (*C*H$_{olef}$), 116.1 (*C*H$_{2,\ olef}$), 34.3 (*C*H$_2$), 29.7 (*C*H$_2$), 25.7 (*C*H$_2$), 15.2 (*C*H$_3$).

The NMR spectroscopic data for the *syn*-configured diastereomer are in accordance with the literature.[167]

***anti*-2-Hydroxy-3-methyl-2-phenylpent-4-enenitrile (234)**



The title compound was prepared according to a modified GP 7 utilizing 26 mg Ni(dppe)Cl_2 (50 μmol, 10 mol%), 6.6 mg zinc powder and 32 mg zinc iodide (100 μmol, 20 mol% each). These materials were suspended in 0.3 mL dichloromethane and 0.2 mL of the $HPPh_2$ solution (0.125 M in dichloromethane, 25 μmol, 5.0 mol%) were added. After cooling to –50 °C, 91.0 mg 2-(but-3-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (0.50 mmol, 1.0 eq) were added. The reaction mixture was stirred for 5 h. Then, 66.0 mg benzoyl cyanide (0.5 mmol, 1.0 eq) were added. The reaction was warmed up to ambient temperature overnight. After general workup and purification by FC (*n*-pentane/Et_2O 3:1) 2-methyl-1,3-diphenylbut-3-en-1-ol (**234**) was obtained as *syn*/*anti* mixture (14:86) in 70% yield (65.0 mg, 0.347 mmol) as colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.57 – 7.52 (m, 2H, C*H*$_{ar}$), 7.45 – 7.38 (m, 3H, C*H*$_{ar}$), 5.78 (ddd, *J* = 17.4, 10.7, 7.2 Hz, 1H, C*H*$_{olef}$), 5.19 (d, *J* = 10.4 Hz, 1H, C*H*$_{2,\ olef}$), 5.10 (d, *J* = 17.2 Hz, 1H, C*H*$_{2,\ olef}$), 4.86 – 4.77 (m, 1H, C*H*), 1.15 (d, *J* = 6.9 Hz, 3H, C*H*$_3$).

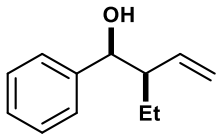
^{13}C NMR (75 MHz, $CDCl_3$) δ 150.6 (*C*H$_{, olef}$), 141.9 (*C*$_{q, ar}$), 128.3 (*C*H$_{ar}$), 128.1 (*C*H$_{ar}$), 127.3 (*C*H$_{ar}$), 127.2 (*C*H$_{ar}$), 126.4 (*C*H$_{ar}$), 126.2 (*C*N), 111.2 (*C*H$_{2, olef}$), 83.2 (*C*H), 29.6 (*C*H), 25.0 (*C*H$_3$).

Resolved signals of the minor diastereomer *syn*-2-hydroxy-3-methyl-2-phenylpent-4-enenitrile:

^{1}H NMR (300 MHz, $CDCl_3$) δ 6.00 – 5.89 (m, 1H, C*H*$_{olef}$), 5.41 – 5.34 (m, 2H, C*H*$_{2, olef}$), 1.00 (d, *J* = 6.9 Hz, 3H, C*H*$_3$).

The NMR spectroscopic data for both diastereomers are in accordance with the literature.[127]

***syn*-2-Ethyl-1-phenylbut-3-en-1-ol (237)**



The title compound was prepared according to a modified GP 7 utilizing 27 mg $Ni(dppp)Cl_2$ (50 μmol, 10 mol%), 6.6 mg zinc powder and 32 mg zinc iodide (100 μmol, 20 mol% each). These materials were suspended in 0.3 mL dichloromethane and 0.2 mL of the $HPPh_2$ solution (0.125 M in dichloromethane, 25 μmol, 5.0 mol%) were added. After cooling to –20 °C, 53 mg benzaldehyde and 98 mg 4,4,5,5-tetramethyl-2-(pent-4-en-1-yl)-1,3,2-dioxaborolane (0.50 mmol, 1.0 eq each) were added. The reaction mixture was stirred for 4 h at –20 °C and overnight at ambient temperature. After general workup and purification by FC (*n*-pentane/Et_2O 10:1) 2-ethyl-1-phenylbut-3-en-1-ol (**237**) was obtained as *syn*/*anti* mixture (91:9) in 72% yield (64 mg, 0.363 mmol) as colorless oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31 – 7.19 (m, 5H, C*H*$_{ar}$), 5.52 – 5.40 (m, 1H, C*H*$_{olef}$), 5.06 – 4.94 (m, 2H, C*H*$_{2, olef}$), 4.59 (d, *J* = 5.9 Hz, 1H, C*H*), 2.33 – 2.23 (m, 1H, C*H*), 2.04 – 1.85 (br s, 1H, O*H*), 1.66 – 1.53 (m, 1H, C*H*$_2$CH$_3$), 1.26 – 1.11 (m, 1H, C*H*$_2$CH$_3$), 0.82 (t, *J* = 7.4 Hz, C*H*$_3$).

^{13}C NMR (125 MHz, $CDCl_3$) δ 142.8 (*C*$_{q, ar}$), 138.4 (*C*H$_{olef}$), 128.2 (*C*H$_{ar}$), 127.5 (*C*H$_{ar}$), 126.9 (*C*H$_{ar}$), 117.6 (*C*H$_{2, olef}$), 76.9 (*C*$_q$), 53.4 (*C*H), 22.7 (*C*H$_2$), 11.9 (*C*H$_3$).

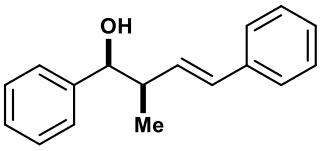
Resolved signals of the minor diastereomer *anti*-2-ethyl-1-phenylbut-3-en-1-ol:

^{1}H NMR (500 MHz, $CDCl_3$) δ 5.68 – 5.56 (m, 1H, C*H*$_{olef}$), 5.25 – 5.13 (m, 2H, C*H*$_{2, olef}$), 4.36 (d, *J* = 8.0 Hz, 1H, C*H*), 2.21 – 2.11 (m, 1H, C*H*), 0.75 (t, *J* = 7.4 Hz, 3H, O*H*).

^{13}C NMR (125 MHz, $CDCl_3$) δ 128.4 (*C*H$_{ar}$), 127.1 (*C*H$_{ar}$), 119.2 (*C*H$_{2, olef}$), 54.8 (*C*H), 23.6 (*C*H$_2$), 13.8 (*C*H$_3$).

The NMR spectroscopic data for both diastereomers are in accordance with the literature.[168]

***syn*-(*E*)-2-Methyl-1,4-diphenylbut-3-en-1-ol (240a)**



The title compound was prepared according to GP 7 utilizing 14 mg Ni(dppp)Cl_2 (25 μmol, 10 mol%), 3.3 mg zinc powder and 16 mg zinc iodide (50 μmol, 20 mol% each). These materials were suspended in 0.15 mL dichloromethane and 0.1 mL of the $HPPh_2$ solution (0.125 M in dichloromethane, 12.5 μmol, 5.0 mol%) were added. After cooling to –20 °C, 27 mg benzaldehyde and 68 mg 4,4,5,5-tetramethyl-2-(1-phenylbut-3-en-1-yl)-1,3,2-dioxaborolane (0.25 mmol, 1.0 eq each) were added. The reaction mixture was stirred for 2 h at –20 °C and overnight at ambient temperature. After general workup and purification by FC (*n*-pentane/Et_2O 8:1) (*E*)-2-methyl-1,4-diphenylbut-3-en-1-ol (**240a**) was obtained as *syn*/*anti* mixture (95:5) in 97% yield (58 mg, 0.243 mmol) as colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.38 – 7.20 (m, 10 H, CH_{ar}), 6.40 (d, *J* = 16.0 Hz, 1H, CH_{olef}), 6.13 (dd, *J* = 16.0 Hz, 8.3 Hz, 1H, CH_{olef}), 4.71 (d, *J* = 5.7 Hz, 1H, C*H*), 2.79 – 2.72 (m, 1H, C*H*), 1.93 (s, 1 H, O*H*), 1.11 (d, *J* = 6.9 Hz, 3H, CH_3).

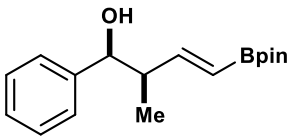
^{13}C NMR (75 MHz, $CDCl_3$) δ 142.7 ($C_{q, ar}$), 132.2 (CH$_{olef}$), 130.9 (CH$_{olef}$), 128.7 (CH$_{ar}$), 128.3 (CH$_{ar}$), 127.6 (CH$_{ar}$), 127.3 (CH$_{ar}$), 126.7 (CH$_{ar}$), 126.3 (CH$_{ar}$), 77.9 (*C*H), 44.3 (*C*H), 15.0 (CH$_3$).

<u>Resolved signals of the minor diastereomer *anti*-(*E*)-2-methyl-1,4-diphenylbut-3-en-1-ol:</u>

^{1}H NMR (300 MHz, $CDCl_3$) δ 6.55 (d, *J* = 15.9 Hz, 1H, CH_{olef}), 6.19 (dd, *J* = 16.0 Hz, 8.3 Hz, 1H, CH_{olef}), 4.47 (d, *J* = 7.9 Hz, 1H, C*H*), 0.98 (d, *J* = 6.9 Hz, 3H, CH_3).

The NMR spectroscopic data for both diastereomers are in accordance with the literature.[169]

***syn*-2-Methyl-1-phenyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)but-3-en-1-ol (240b)**



The title compound was prepared according to GP 7 utilizing 27 mg Ni(dppp)Cl_2 (50 μmol, 10 mol%), 6.6 mg zinc powder and 32 mg zinc iodide (100 μmol, 20 mol% each). These materials were suspended in 0.3 mL dichloromethane and 0.2 mL of the $HPPh_2$ solution (0.125 M in dichloromethane, 25 μmol, 5.0 mol%) were added. 53 mg benzaldehyde and 154 mg 2,2'-(but-3-en-1,1-diyl)-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (0.50 mmol, 1.0 eq each) were added. The

reaction mixture was stirred overnight at ambient temperature. After general workup and purification by FC (*n*-pentane/Et_2O 20:1) 2-methyl-1-phenyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)but-3-en-1-ol (**240b**) was obtained as *syn*/*anti* mixture (76:24) in 71% yield (102 mg, 0.354 mmol) as colorless liquid.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.37 – 7.29 (m, 5H, CH_{ar}), 6.66 (dd, *J* = 18.0, 6.6 Hz, 1H, CH_{olef}), 5.50 (dd, *J* = 18.0, 1.4 Hz, 1H, CH_{olef}), 4.76 (t, *J* = 4.0 Hz, 1H, C*H*), 2.64 (tq, *J* = 6.6, 1.9 Hz, 1H, C*H*), 1.82 (d, *J* = 3.4 Hz, 1H, O*H*), 1.26 (s, 12H, C$H_{3,\ pin}$), 0.96 (d, *J* = 6.8 Hz, 3H, CH_3).

^{13}C NMR (75 MHz, $CDCl_3$) δ 155.7 (*C*H_{olef}), 142.8 ($C_{q,\ ar}$), 128.2 (*C*H_{ar}), 127.4 (*C*H_{ar}), 126.4 (*C*H_{ar}), 83.3 ($C_{q,\ pin}$), 76.7 (*C*H), 46.5 (*C*H), 24.9 (*C*$H_{3,\ pin}$), 12.9 (*C*H_3). B*C*H not detectable.

^{11}B NMR (96 MHz, $CDCl_3$) δ 30.01 (*B*pin).

IR (neat) 3477, 3028, 2976, 2930, 2874, 1726, 1635, 1493, 1452, 1390, 1356, 1318, 1271, 1212, 1165, 1142, 1108, 1073, 1042, 1001, 968, 933, 913, 898, 849, 751, 700, 673, 578, 531.

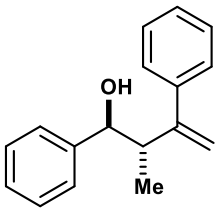
HRMS (EI) calculated for $C_{16}H_{22}BO_3$ ($M^+ - CH_3$): *m*/*z* = 273.1665; found *m*/*z* = 273.1644.

Resolved signals of the minor diastereomer *anti*-2-methyl-1-phenyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)but-3-en-1-ol:

^{1}H NMR (300 MHz, $CDCl_3$) δ 5.62 (dd, 1 H, *J* = 18.1, 0.8 Hz, CH_{olef}).

^{13}C NMR (75 MHz, $CDCl_3$) δ 131.0 (*C*H_{olef}), 48.2 (*C*H), 15.4 (*C*H_3).

***anti*-2-Methyl-1,3-diphenylbut-3-en-1-ol (240c)**



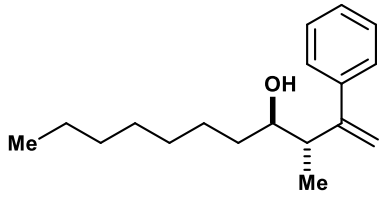
The title compound was prepared according to GP 7 utilizing 26 mg $Ni(dppe)Cl_2$ (50 μmol, 10 mol%), 6.6 mg zinc powder and 32 mg zinc iodide (100 μmol, 20 mol% each). These materials were suspended in 0.3 mL dichloromethane and 0.2 mL of the $HPPh_2$ solution (0.125 M in dichloromethane, 25 μmol, 5.0 mol%) were added. 53 mg benzaldehyde and 129 mg 4,4,5,5-tetramethyl-2-(2-phenylbut-3-en-1-yl)-1,3,2-dioxaborolane (0.50 mmol, 1.0 eq each) were added. The reaction mixture was stirred overnight at ambient temperature. After general workup and purification by FC (*n*-pentane/Et_2O 3:1) *anti*-2-methyl-1,3-diphenylbut-3-en-1-ol (**240c**) was obtained in 71% yield (84 mg, 0.352 mmol) as colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35 – 7.16 (m, 10H, CH_{ar}), 5.37 (s, 1H, CH_{olef}), 5.18 (s, 1H, CH_{olef}), 4.67 – 4.66 (m, 1H, C*H*), 3.15 – 3.07 (m, 1H, C*H*), 1.76 (d, 1H, O*H*), 1.05 (d, *J* = 6.9 Hz, 3H, CH_3).

^{13}C NMR (75 MHz, $CDCl_3$) δ 152.0 ($C_{q, olef}$), 143.1 ($C_{q, ar}$), 142.5 ($C_{q, ar}$), 128.6 (CH_{ar}), 128.2 (CH_{ar}), 127.8 (CH_{ar}), 127.2 (CH_{ar}), 126.9 (CH_{ar}), 126.1 (CH_{ar}), 114.3 ($CH_{2, olef}$), 74.2 (*C*H), 45.6 (*C*H), 12.4 (CH_3).

The NMR spectroscopic data are in accordance with the literature.[170]

anti-3-Methyl-2-phenylundec-1-en-4-ol (240d)



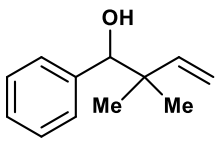
The title compound was prepared according to GP 7 utilizing 26 mg $Ni(dppe)Cl_2$ (50 μmol, 10 mol%), 6.6 mg zinc powder and 32 mg zinc iodide (100 μmol, 20 mol% each). These materials were suspended in 0.3 mL dichloromethane and 0.2 mL of the $HPPh_2$ solution (0.125 M in dichloromethane, 25 μmol, 5.0 mol%) were added. 52 mg octanal and 129 mg 4,4,5,5-tetramethyl-2-(2-phenylbut-3-en-1-yl)-1,3,2-dioxaborolane (0.50 mmol, 1.0 eq each) were added. The reaction mixture was stirred overnight at ambient temperature. After general workup and purification by FC (*n*-pentane/Et_2O 10:1) *anti*-3-methyl-2-phenylundec-1-en-4-ol (**240d**) was obtained in 41% yield (53 mg, 0.210 mmol) as colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.27 – 7.17 (m, 5H, CH_{ar}), 5.29 – 5.28 (m, 1H, CH_{olef}), 5.05 – 5.04 (s, 1H, CH_{olef}), 3.45 – 3.39 (m, 1H, C*H*), 2.81 – 2.74 (m, 1H, C*H*), 1.39 – 1.09 (m, 15H, O*H*), 0.78 (d, *J* = 6.9 Hz, 3H, CH_3).

^{13}C NMR (75 MHz, $CDCl_3$) δ 152.7 ($C_{q, olef}$), 142.6 ($C_{q, ar}$), 142.5 ($C_{q, ar}$), 128.7 (CH_{ar}), 128.6 (CH_{ar}), 127.7 (CH_{ar}), 126.9 (CH_{ar}), 126.8 (CH_{ar}), 126.1 (CH_{ar}), 113.6 ($CH_{2, olef}$), 74.2 (*C*H), 43.1 (*C*H), 34.8 (CH_2), 32.0 (CH_2), 29.8 (CH_2), 29.4 (CH_2), 26.5 (CH_2), 22.8 (CH_2), 14.2 (CH_3), 12.4 (CH_3).

The NMR spectroscopic data are in accordance with the literature.[170]

2,2-Dimethyl-1-phenylbut-3-en-1-ol (247a)



The title compound was prepared according to GP 8 utilizing 16 mg $Ni(dppp)Br_2$ (25 μmol, 10 mol%), 3.3 mg zinc powder and 16 mg zinc iodide (50 μmol, 20 mol% each). These materials were suspended in 0.15 mL

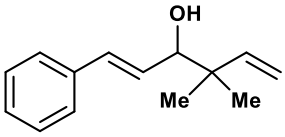
dichloromethane and 0.1 mL of the $HPPh_2$ solution (0.125 M in dichloromethane, 12.5 μmol, 5.0 mol%) were added. After stirring for additional 10 min at ambient temperature, 49 mg 4,4,5,5-tetramethyl-2-(3-methylbut-3-en-1-yl)-1,3,2-dioxaborolane (0.25 mmol, 1.0 eq) were added. The reaction mixture was stirred overnight at ambient temperature. Then, 27 mg benzaldehyde (0.25 mmol, 1.0 eq) were added. After further stirring overnight, general workup and purification by FC (*n*-pentane/Et_2O 10:1) 2,2-dimethyl-1-phenylbut-3-en-1-ol (**247a**) was obtained in 75% yield (33 mg, 0.187 mmol) as colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.31 – 7.27 (m, 5H, CH_{ar}), 5.92 (dd, *J* = 17.5, 10.8 Hz, 1H, CH_{olef}), 5.15 (dd, *J* = 10.7, 1.2 Hz, 1H, CH_{olef}), 5.09 (dd, *J* = 17.5, 1.4 Hz, 1H, CH_{olef}), 4.44 (s, 1H, C*H*), 2.00 (s, 1 H, O*H*), 1.02 (s, 3H, CH_3), 0.97 (s, 3 H, CH_3).

^{13}C NMR (75 MHz, $CDCl_3$) δ 145.3 (*C*H_{olef}), 141.0 ($C_{q, ar}$), 128.0 (*C*H_{ar}), 127.7 (*C*H_{ar}), 127.6 (*C*H_{ar}), 114.0 (*C*$H_{2, olef}$), 80.9 (*C*H), 42.5 (*C*$(CH_3)_2$), 24.7 (*C*H_3), 21.3 (*C*H_3).

The NMR spectroscopic data are in accordance with the literature.[171]

4,4-Dimethyl-1-phenylhexa-1,5-dien-3-ol (247b)



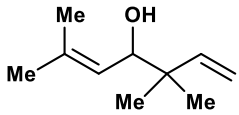
The title compound was prepared according to GP 8 utilizing 14 mg Ni(dppp)Cl_2 (25 μmol, 10 mol%), 3.3 mg zinc powder and 16 mg zinc iodide (50 μmol, 20 mol% each). These materials were suspended in 0.15 mL dichloromethane and 0.1 mL of the $HPPh_2$ solution (0.125 M in dichloromethane, 12.5 μmol, 5.0 mol%) were added. After stirring for additional 10 min at ambient temperature, 49 mg 4,4,5,5-tetramethyl-2-(3-methylbut-3-en-1-yl)-1,3,2-dioxaborolane (0.25 mmol, 1.0 eq) were added. The reaction mixture was stirred overnight at ambient temperature. Then, 33 mg cinnamaldehyde (0.25 mmol, 1.0 eq) were added. After further stirring overnight, general workup and purification by FC (*n*-pentane/Et_2O 8:1) 4,4-dimethyl-1-phenylhexa-1,5-dien-3-ol (**247b**) was obtained in 81% yield (41 mg, 0.203 mmol) as colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.46 – 7.29 (m, 5 H, CH_{ar}), 6.60 (d, *J* = 15.9 Hz, 1H, CH_{olef}), 6.25 (dd, *J* = 15.9 Hz, 7.0 Hz, 1H, CH_{olef}), 5.93 (dd, *J* = 17.4 Hz, 10.8 Hz, 1H, CH_{olef}), 5.15 (dd, *J* = 8.4, 1.3 Hz, 1H, CH_{olef}), 5.11 (dd, *J* = 15.1, 1.3 Hz, 1H, CH_{olef}), 3.99 (d, *J* = 6.6 Hz, 1H, C*H*), 1.69 (s, 1H, O*H*), 1.09 (s, 3 H, CH_3), 1.07 (s, 3 H, CH_3).

^{13}C NMR (75 MHz, $CDCl_3$) δ 145.1 (*C*H$_{olef}$), 137.0 ($C_{q, ar}$), 132.3 (*C*H$_{olef}$), 128.9 (*C*H$_{ar}$), 128.6 (*C*H$_{ar}$), 127.8 (*C*H$_{ar}$), 126.7 (*C*H$_{olef}$), 114.0 (*C*H$_{2, olef}$), 79.5 (C_q), 42.1 (*C*H), 24.0 (*C*H$_3$), 22.0 (*C*H$_3$).

The NMR spectroscopic data are in accordance with the literature.[165,172]

Artemisia Alcohol (247c)



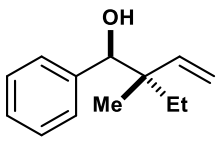
The title compound was prepared according to GP 8 utilizing 16 mg Ni(dppp)Br_2 (25 μmol, 10 mol%), 3.3 mg zinc powder and 16 mg zinc iodide (50 μmol, 20 mol% each). These materials were suspended in 0.15 mL dichloromethane and 0.1 mL of the $HPPh_2$ solution (0.125 M in dichloromethane, 12.5 μmol, 5.0 mol%) were added. After stirring for additional 10 min at ambient temperature, 49 mg 4,4,5,5-tetramethyl-2-(3-methylbut-3-en-1-yl)-1,3,2-dioxaborolane (0.25 mmol, 1.0 eq) were added. The reaction mixture was stirred overnight at ambient temperature. Then, 21 mg 3-methylcrotonaldehyde (0.25 mmol, 1.0 eq) were added. After further stirring overnight, general workup and purification by FC (*n*-pentane/Et_2O 20:1) artemisia alcohol (**247c**) was obtained in 80% yield (31 mg, 0.200 mmol) as colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ 5.89 (dd, *J* = 17.5 Hz, 10.9 Hz, 1H, C*H*$_{olef}$), 5.21 – 5.16 (m, 1H, C*H*$_{olef}$), 5.10 (dd, *J* = 7.4, 1.5 Hz, 1H, C*H*$_{olef}$), 5.06 (dd, *J* = 14.1, 1.5 Hz, 1H, C*H*$_{olef}$), 4.05 (d, *J* = 9.3 Hz, 1H, C*H*), 1.75 (s, 3H, C*H*$_3$), 1.70 (s, 3H, C*H*$_3$), 1.01 (s, 3H, C*H*$_3$), 0.99 (s, 3H, C*H*$_3$).

^{13}C NMR (75 MHz, $CDCl_3$) δ 145.4 (*C*H$_{olef}$), 136.7 ($C_{q, olef}$), 124.3 (*C*H$_{olef}$), 113.5 (*C*H$_{2, olef}$), 74.8 (*C*H), 42.1 (*C*(CH$_3$)$_2$), 26.2 (*C*H$_3$), 24.1 (*C*H$_3$), 21.4 (*C*H$_3$), 18.6 (*C*H$_3$).

The NMR spectroscopic data are in accordance with the literature.[173]

***anti*-2-Ethyl-2-methyl-1-phenylbut-3-en-1-ol (130)**



The title compound was prepared according to GP 8 utilizing 15 mg Ni(dppm)Br_2 (25 μmol, 10 mol%), 3.3 mg zinc powder and 16 mg zinc iodide (50 μmol, 20 mol% each). These materials were suspended in 0.15 mL dichloromethane and 0.1 mL of the $HPPh_2$ solution (0.125 M in dichloromethane, 12.5 μmol, 5.0 mol%) were added. After stirring for additional 10 min at ambient temperature, 53 mg 4,4,5,5-tetramethyl-2-(3-methylenepentyl)-1,3,2-dioxaborolane (0.25 mmol, 1.0 eq) were added. The reaction mixture was stirred 2 d at ambient temperature. Then, 27 mg benzaldehyde (0.25 mmol, 1.0 eq) were added. After further stirring overnight, general workup

and purification by FC (*n*-pentane/Et_2O 10:1) 2-ethyl-2-methyl-1-phenylbut-3-en-1-ol (**130**) was obtained as *syn*/*anti* mixture (19:81) in 43% yield (21 mg, 0.108 mmol) as colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.32 – 7.26 (m, 5H, CH_{ar}), 5.83 (dd, *J* = 17.7 Hz, 10.8 Hz, 1H, CH_{olef}), 5.29 (dd, *J* = 10.9, 1.4 Hz, 1H, CH_{olef}), 5.08 (dd, *J* = 16.3, 1.4 Hz, 1H, CH_{olef}), 4.44 (s, 1H, C*H*), 2.02 (d, *J* = 2.0 Hz, 1H, O*H*), 1.54 – 1.22 (m, 2H, CH_2), 0.88 (s, 3H, CH_3), 0.78 (t, *J* = 7.5 Hz, 3H, CH_3).

^{13}C NMR (125 MHz, $CDCl_3$) δ 144.0 (*C*H_{olef}), 128.2 (*C*H_{ar}), 127.6 (*C*H_{ar}), 116.1 (*C*$H_{2,\ olef}$), 80.2 (*C*H), 46.3 (C_q), 30.1 (*C*H_2), 15.9 (*C*H_3), 8.5 (*C*H_3).

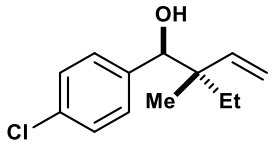
Resolved signals of the minor diastereomer *syn*-2-ethyl-2-methyl-1-phenylbut-3-en-1-ol:

^{1}H NMR (300 MHz, $CDCl_3$) δ 5.75 (dd, *J* = 17.5, 10.2 Hz, 1H, CH_{olef}), 5.20 (dd, *J* = 10.8, 1.5 Hz, 1H, CH_{olef}), 5.01 (dd, *J* = 17.7, 1.5 Hz, 1H, CH_{olef}), 4.46 (s, 1H, C*H*), 1.05 (s, 3H, CH_3).

^{13}C NMR (125 MHz, $CDCl_3$) δ 142.6 (CH_{olef}), 128.0 (CH_{ar}), 127.6 (CH_{ar}), 115.5 (C$H_{2,\ olef}$), 80.9 (C*H*), 29.0 (CH_2), 18.7 (CH_3).

The NMR spectroscopic data for the *syn*-configured diastereomer are in accordance with the literature.[78]

***anti*-1-(4-Chlorophenyl)-2-ethyl-2-methylbut-3-en-1-ol (247d)**



The title compound was prepared according to GP 8 utilizing 15 mg Ni(dppm)Br_2 (25 μmol, 10 mol%), 3.3 mg zinc powder and 16 mg zinc iodide (50 μmol, 20 mol% each). These materials were suspended in 0.15 mL dichloromethane and 0.1 mL of the $HPPh_2$ solution (0.125 M in dichloromethane, 12.5 μmol, 5.0 mol%) were added. After stirring for additional 10 min at ambient temperature, 53 mg 4,4,5,5-tetramethyl-2-(3-methylenepentyl)-1,3,2-dioxaborolane (0.25 mmol, 1.0 eq) were added. The reaction mixture was stirred 2 d at ambient temperature. Then, 35 mg 4-chlorobenzaldehyde (0.25 mmol, 1.0 eq) were added. After further stirring overnight, general workup and purification by FC (*n*-pentane/Et_2O 10:1) 1-(4-chlorophenyl)-2-ethyl-2-methylbut-3-en-1-ol (**247d**) was obtained as *syn*/*anti* mixture (33:67) in 73% yield (41 mg, 0.182 mmol) as colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.34 – 7.23 (m, 4H, CH_{ar}), 5.83 (dd, *J* = 17.6 Hz, 11.0 Hz, 1H, CH_{olef}), 5.34 (d, *J* = 10.8 Hz, 1H, CH_{olef}), 5.14 (d, *J* = 17.6 Hz, 1H, CH_{olef}), 4.46 (s, 1H, C*H*), 2.05 (s, 1H, O*H*), 1.56 – 1.24 (m, 2H, CH_2), 0.90 (s, 3H, CH_3), 0.83 (t, 3H, *J* = 7.4 Hz, CH_3).

^{13}C NMR (75 MHz, $CDCl_3$) δ 143.6 (CH_{olef}), 139.2 ($C_{q, ar}$), 133.3 ($C_{q, ar}$), 129.5 (CH_{ar}), 127.8 (CH_{ar}), 116.5 ($CH_{2, olef}$), 79.5 (*C*H), 46.3 (C_q), 30.1 (CH_2), 15.8 (CH_3), 8.4 (CH_3).

IR (neat) 3453, 2969, 2937, 2878, 1637, 1489, 1459, 1412, 1379, 1185, 1090, 1068, 1031, 910, 831, 788, 751, 733, 677, 544, 467.

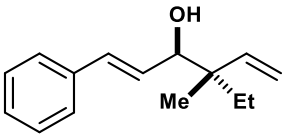
HRMS (EI) calculated for C_7H_6ClO (fragment): *m*/*z* = 141.0095; found *m*/*z* = 141.0107.

Resolved signals of the minor diastereomer *syn*-1-(4-chlorophenyl)-2-ethyl-2-methylbut-3-en-1-ol:

^{1}H NMR (300 MHz, $CDCl_3$) δ 5.75 (dd, *J* = 17.5, 10.9 Hz, 1H, CH_{olef}), 5.25 (d, *J* = 11.0 Hz, 1H, CH_{olef}), 5.04 (d, *J* = 17.6 Hz, 1H, CH_{olef}), 4.48 (s, 1H, C*H*), 1.06 (s, 3H, CH_3).

^{13}C NMR (75 MHz, $CDCl_3$) δ 142.3 (CH_{olef}), 140.0 ($C_{q, ar}$), 133.2 ($C_{q, ar}$), 129.3 (CH_{ar}), 127.7 (CH_{ar}), 115.8 ($CH_{2, olef}$), 80.2 (*C*H), 45.7 (C_q), 28.9 (CH_2), 18.5 (CH_3).

***anti*-4-Ethyl-4-methyl-1-phenylhexa-1,5-dien-3-ol (247e)**



The title compound was prepared according to GP 8 utilizing 15 mg Ni(dppm)Br_2 (25 μmol, 10 mol%), 3.3 mg zinc powder and 16 mg zinc iodide (50 μmol, 20 mol% each). These materials were suspended in 0.15 mL dichloromethane and 0.1 mL of the $HPPh_2$ solution (0.125 M in dichloromethane, 12.5 μmol, 5.0 mol%) were added. After stirring for additional 10 min at ambient temperature, 52 mg 4,4,5,5-tetramethyl-2-(3-methylenepentyl)-1,3,2-dioxaborolane (0.25 mmol, 1.0 eq each) were added. The reaction mixture was stirred 2 d at ambient temperature. Then, 33 mg cinnamaldehyde were added and stirring was continued for another day. After general workup and purification by FC (*n*-pentane/Et_2O 12:1) 4-ethyl-4-methyl-1-phenylhexa-1,5-dien-3-ol (**247e**) was obtained as *syn*/*anti* mixture (23:77) in 67% yield (36 mg, 0.167 mmol) as colorless oil. The product mixture contained 11 mg (20%) of unreacted cinnamaldehyde which could not be removed by multiple column chromatography.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.59 – 7.21 (m, 5H, CH_{ar}), 6.60 (d, *J* = 15.8 Hz, 1H, CH_{olef}), 6.21 (dd, *J* = 15.9, 7.4 Hz, 1H, CH_{olef}), 5.82 (dd, *J* = 17.6, 10.9 Hz, 1H, CH_{olef}), 5.27 (dd, *J* = 10.8, 1.4 Hz, 1H, CH_{olef}), 5.11 (dd, *J* = 17.6, 1.5 Hz, 1H, CH_{olef}), 4.00 (d, *J* = 7.3 Hz, 1H, C*H*), 1.71 (s, 1H, O*H*), 1.47 (q, *J* = 7.4 Hz, 2H, CH_2), 0.99 (s, 3H, CH_3), 0.83 (t, *J* = 7.5 Hz, 3H, CH_3).

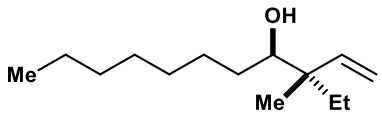
^{13}C NMR (75 MHz, $CDCl_3$) δ 152.8 (*C*H$_{olef}$), 143.8 ($C_{q,\ ar}$), 131.4 (*C*H$_{olef}$), 128.9 (*C*H$_{ar}$), 128.7 (*C*H$_{ar}$), 127.8 (*C*H$_{ar}$), 126.7 (*C*H$_{olef}$), 115.8 (*C*H$_{2,\ olef}$), 78.6 (*C*H), 45.7 (C_q), 30.1 (*C*H$_2$), 16.8 (*C*H$_3$), 8.4 (*C*H$_3$).

Resolved signals of the minor diastereomer *syn*-4-ethyl-4-methyl-1-phenylhexa-1,5-dien-3-ol:

^{1}H NMR (300 MHz, $CDCl_3$) δ 6.59 (d, *J* = 15.8 Hz, 1H, C*H*$_{olef}$), 5.22 (dd, *J* = 10.9, 1.5 Hz, 1H, C*H*$_{olef}$), 5.08 (dd, *J* = 17.5, 1.5 Hz, 1H, C*H*$_{olef}$), 1.06 (s, 3H, C*H*$_3$), 0.84 (t, *J* = 7.5 Hz, 3H, C*H*$_3$).

The NMR spectroscopic data are in accordance with the literature.[174]

***anti*-3-Ethyl-3-methylundec-1-en-4-ol (247f)**



The title compound was prepared according to GP 8 utilizing 15 mg Ni(dppm)Br_2 (25 μmol, 10 mol%), 3.3 mg zinc powder and 16 mg zinc iodide (50 μmol, 20 mol% each). These materials were suspended in 0.15 mL dichloromethane and 0.1 mL of the $HPPh_2$ solution (0.125 M in dichloromethane, 12.5 μmol, 5.0 mol%) were added. After stirring for additional 10 min at ambient temperature, 53 mg 4,4,5,5-tetramethyl-2-(3-methylenepentyl)-1,3,2-dioxaborolane (0.25 mmol, 1.0 eq each) were added. The reaction mixture was stirred overnight at ambient temperature. Then, 32 mg octanal were added and stirring was continued for another day. After general workup and purification by FC (*n*-pentane/Et_2O 30:1) 3-ethyl-3-methylundec-1-en-4-ol (**247f**) was obtained as *syn*/*anti* mixture (31:69) in 52% yield (28 mg, 0.131 mmol) as colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ 5.73 (dd, *J* = 17.6, 10.9 Hz, 1H, C*H*$_{olef}$), 5.20 (dd, *J* = 10.9, 1.6 Hz, 1H, C*H*$_{olef}$), 5.04 (dd, *J* = 17.6, 1.6 Hz, 1H, C*H*$_{olef}$), 3.27 (d, *J* = 10.0 Hz, 1H, C*H*), 1.59 – 1.37 (m, 2H, C*H*$_2$), 1.28 (s, 12H, C*H*$_2$), 0.92 (s, 3H, C*H*$_3$), 0.88 (t, *J* = 7.0 Hz, 3H, C*H*$_3$), 0.79 (t, *J* = 7.5 Hz, 3H, C*H*$_3$).

^{13}C NMR (75 MHz, $CDCl_3$) δ 144.4 (*C*H$_{olef}$), 115.3 (*C*H$_{2,\ olef}$), 78.1 (*C*H), 45.4 (C_q), 32.03 (*C*H$_2$), 31.1 (*C*H$_2$), 29.9 (*C*H$_2$), 29.78 (*C*H$_2$), 29.7 (*C*H$_2$), 29.5 (*C*H$_2$), 27.3 (*C*H$_2$), 16.4 (*C*H$_3$), 14.2 (*C*H$_3$), 8.5 (*C*H$_3$).

IR (neat) = 3405, 2959, 2922, 2873, 2855, 1461, 1413, 1378, 1308, 1119, 1038, 911, 683, 442.

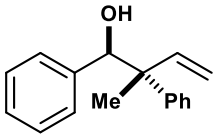
HRMS (EI) calculated for $C_{14}H_{28}O$: *m*/*z* = 212.2140; found *m*/*z* = 212.2151.

Resolved signals of the minor diastereomer *syn*-3-ethyl-3-methylundec-1-en-4-ol:

^{1}H NMR (300 MHz, $CDCl_3$) δ 5.68 (dd, *J* = 17.6, 10.9 Hz, 1H), 5.14 (dd, *J* = 11.0, 1.5 Hz, 1H), 4.99 (dd, *J* = 17.6, 1.6 Hz, 1H), 3.29 (d, *J* = 10.2 Hz, 1H), 0.96 (s, 3H), 0.81 (t, *J* = 7.5 Hz, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 143.7 (CH_{olef}), 114.6 ($CH_{2,\ olef}$), 45.1 (C_q), 32.00 (CH_2), 29.80 (CH_2), 27.2 (CH_2), 17.4 (CH_3), 8.4 (CH_3).

anti-2-Methyl-1,2-diphenylbut-3-en-1-ol (247g)



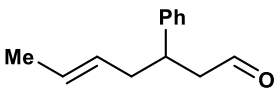
The title compound was prepared according to GP 8 utilizing 14 mg Ni(dppe)Cl_2 (25 μmol, 10 mol%), 3.3 mg zinc powder and 16 mg zinc iodide (50 μmol, 20 mol% each). These materials were suspended in 0.15 mL acetonitrile and 0.1 mL of the $HPPh_2$ solution (0.125 M in acetonitrile, 12.5 μmol, 5.0 mol%) were added. At ambient temperature 27 mg benzaldehyde and 65 mg 4,4,5,5-tetramethyl-2-(3-phenylbut-3-en-1-yl)-1,3,2-dioxaborolane (0.25 mmol, 1.0 eq each) were added. The reaction mixture was stirred overnight at 80 °C. After general workup and purification by FC (*n*-pentane/Et_2O 8:1) 2-methyl-1,2-diphenylbut-3-en-1-ol (**247g**) was obtained as *syn*/*anti* mixture (3:97) in 63% yield (38 mg, 0.158 mmol) as colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.40 – 7.10 (m, 10H, CH_{ar}), 6.61 – 6.51 (m, 1H, CH_{olef}), 5.34 – 5.31 (m, 1H, CH_{olef}), 5.14 – 5.07 (m, 2H, CH_{olef} + C*H*), 2.05 (s, 1H, O*H*), 1.30 (s, 3H, CH_3).

^{13}C NMR (75 MHz, $CDCl_3$) δ 148.9 (CH_{olef}), 141.2 ($C_{q,\ ar}$), 140.3 ($C_{q,\ ar}$), 128.5 (CH_{ar}), 128.1 (CH_{ar}), 127.6 (CH_{ar}), 127.5 (CH_{ar}), 127.4 (CH_{ar}), 126.7 (CH_{ar}), 115.8 ($CH_{2,\ olef}$), 80.5 (*C*H), 50.5 (C_q), 20.8 (CH_3).

The NMR spectroscopic data are in accordance with the literature.[165]

(*E*/*Z*)-3-Phenylhept-5-enal (248a)



The title compound was prepared according to a modified GP 8 utilizing 27 mg Ni(dppp)Cl_2 (50 μmol, 10 mol%), 6.6 mg zinc powder and 32 mg zinc iodide (100 μmol, 20 mol% each). These materials were suspended in 0.3 mL dichloromethane and 0.2 mL of the $HPPh_2$ solution (0.125 M in dichloromethane, 25 μmol, 5.0 mol%) were added. After cooling to –40 °C, 66 mg cinnamaldehyde and 91 mg 2-(but-3-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (0.5 mmol, 1.0 eq each) were added. The reaction mixture was stirred for 6 h at –40 °C. Then, 0.5 mL anhydrous THF were added as well as 380 mg [18]-crown-6 (1.48 mmol, 3.0 eq) and 39 mg potassium hydride (0.99 mmol,

2.0 eq). The reaction mixture was stirred overnight at ambient temperature before being quenched with water. The aqueous layer was extracted with Et_2O. The organic layer was washed with brine, dried over $MgSO_4$, filtered and the solvent was evaporated. After purification by FC (*n*-pentane/Et_2O 10:1) 3-phenylhept-5-enal (**248a**) was obtained as *E/Z* mixture (90:10) in 47% yield (43 mg, 0.230 mmol) as colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ 9.66 (t, *J* = 2.0 Hz, 1H, C*H*O), 7.32 – 7.16 (m, 5H, CH_{ar}), 5.49 – 5.40 (m, 1H, CH_{olef}), 5.32 – 5.25 (m, 1H, CH_{olef}), 3.27 – 3.21 (m, 1H, C*H*), 2.74 (dd, *J* = 6.3, 2.2 Hz, 1H, CH_2), 2.70 (dd, *J* = 8.3, 2.2 Hz, 1H, CH_2), 2.39 – 2.26 (m, 2H, CH_2), 1.62 (dd, *J* = 6.4, 1.0 Hz, 3H, CH_3).

^{13}C NMR (75 MHz, $CDCl_3$) δ 202.2 (*C*HO), 143.9 ($C_{q, ar}$), 128.7 (*C*H_{ar}), 128.1 (*C*H_{olef}), 127.6 (*C*H_{olef}), 49.4 (*C*H_2), 40.4 (*C*H), 40.0 (*C*H_2), 18.0 (*C*H_3).

IR (neat) 3062, 2916, 2722, 1722, 1686, 1494, 1452, 1377, 967, 758, 699, 537.

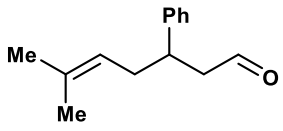
HRMS (EI) calculated for $C_{13}H_{16}O$: *m*/*z* = 188.1201; found *m*/*z* = 188.1211.

Resolved signals of the minor isomer (*Z*)-3-phenylhept-5-enal:

^{1}H NMR (300 MHz, $CDCl_3$) δ 9.68 (t, *J* = 2.1 Hz, 1H, C*H*O), 1.54 (d, *J* = 6.8 Hz, 3H, CH_3).

^{13}C NMR (75 MHz, $CDCl_3$) δ 202.0 (*C*HO), 143.8 ($C_{q, ar}$), 128.7 (*C*H_{ar}), 128.0 (*C*H_{olef}), 127.5 (*C*H_{olef}), 49.5 (*C*H_2), 18.1 (*C*H_3).

6-Methyl-3-phenylhept-5-enal (248b)



The title compound was prepared according to a modified GP 8 utilizing 14 mg Ni(dppp)Cl_2 (25 µmol, 10 mol%), 3.3 mg zinc powder and 16 mg zinc iodide (50 µmol, 20 mol% each). These materials were suspended in 0.15 mL dichloromethane and 0.1 mL of the $HPPh_2$ solution (0.125 m in dichloromethane, 12.5 µmol, 5.0 mol%) were added. After stirring for additional 10 min at ambient temperature, 49 mg 4,4,5,5-tetramethyl-2-(3-methylbut-3-en-1-yl)-1,3,2-dioxaborolane (0.25 mmol, 1.0 eq) were added. The reaction mixture was stirred overnight at ambient temperature. Then, 33 mg cinnamaldehyde (0.25 mmol, 1.0 eq), 0.5 mL anhydrous THF were added as well as 182 mg [18]-crown-6 (0.69 mmol, 3.0 eq) and 19 mg potassium hydride (0.46 mmol, 2.0 eq). The reaction mixture was stirred overnight at ambient temperature before being quenched with water. The aqueous layer was extracted with Et_2O. The organic layer was washed with brine, dried over $MgSO_4$, filtered and the solvent was evaporated. After

purification by FC (*n*-pentane/Et_2O 10:1) 6-methyl-3-phenylhept-5-enal (**248b**) was obtained in 23% yield (12 mg, 0.060 mmol) as colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ 9.66 (t, *J* = 2.0 Hz, 1H, C*H*O), 7.33 – 7.18 (m, 5H, CH_{ar}), 5.04 (t, *J* = 7.0 Hz, 1H, CH_{olef}), 3.27 – 3.18 (m, 1H, C*H*), 2.74 – 2.70 (m, 2H, CH_2), 2.40 – 2.27 (m, 2H, CH_2), 1.66 (s, 3H, CH_3), 1.54 (s, 3H, CH_3).

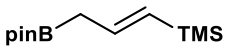
^{13}C NMR (75 MHz, $CDCl_3$) δ 202.1 (*C*HO), 134.2 ($C_{q, ar}$), 128.7 (*C*H_{ar}), 127.6 (*C*H_{ar}), 126.7 (*C*H_{ar}), 121.7 (*C*H_{ar}), 49.5 (*C*H_2), 40.7 (*C*H), 35.5 (*C*H_2), 25.9 (*C*H_3), 18.0 (*C*H_3).

IR (neat) 2967, 2914, 2782, 2251, 1722, 1495, 1452, 1377, 910, 731, 699, 541.

HRMS (EI) calculated for $C_{14}H_{18}O$: *m*/*z* = 202.1400; found *m*/*z* = 202.1342.

5.6 Cobalt-Catalyzed Reductive Cyclization

(*E*)-Trimethyl(3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)prop-1-en-1-yl)silane (268)



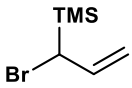
According to a procedure of Stupp,[131] 15.4 mL *s*-BuLi (1.3 M in *n*-hexane, 20.0 mmol, 1.0 eq) and 3.0 mL TMEDA (20.0 mmol, 1.0 eq) were dissolved in 20 mL anhydrous THF. Then, 3.2 mL allyl bromide (20 mmol, 1.0 eq) were added at −78 °C. The reaction was stirred at −40 °C for 2 h. A solution of 4.0 mL *i*PrOBpin (20.0 mmol, 1.0 eq) in 5.0 mL anhydrous THF was precooled to −78 °C before being added to the reaction mixture. The reaction was stirred overnight at ambient temperature and then quenched with aqueous NH_4Cl solution. The aqueous layer was extracted three times with Et_2O, the organic layer was dried over $MgSO_4$, filtered and the solvent was evaporated. After purification by FC (*n*-pentane/Et2O 25:1) (*E*)-trimethyl(3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)prop-1-en-1-yl)silane (**268**) was obtained in 48% yield (2.27 g, 9.50 mmol) as colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ 6.07 (dt, *J* = 18.5, 7.5 Hz, 1H, C*H*$_{olef}$), 5.63 (d, *J* = 18.5 Hz, 1H, C*H*$_{olef}$), 1.80 (d, *J* = 7.0 Hz, 2H, C*H*$_2$), 1.24 (s, 12H, C*H*$_{3,\ pin}$), 0.03 (s, 9H, Si(C*H*$_3$)$_3$).

^{13}C NMR (75 MHz, $CDCl_3$) δ 142.0 (*C*H$_{olef}$), 130.7 (*C*H$_{olef}$), 83.2 (*C*H$_2$), 24.7 (*C*H$_{3,\ pin}$), –1.1 (Si(*C*H$_3$)$_3$).

The NMR spectroscopic data are in accordance with the literature.[131]

(1-Bromoallyl)trimethylsilane (272)



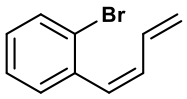
According to a procedure of Gennari,[175] 10.4 mL *n*-BuLi (2.5 M in *n*-hexane, 24.0 mmol, 1.2 eq) were added to a solution of di*iso*propylamine (3.64 mL, 26 mmol, 1.3 eq) in 6 mL anhydrous THF at –78 °C. After stirring at 0 °C for 30 min, the solution was added to a mixture of allyl bromide (2.08 mL, 24 mmol, 1.2 eq) and TMSCl (2.52 mL, 20 mmol, 1.0 eq) in 5 mL anhydrous THF at –78 °C. After stirring for 1 h, the reaction was quenched with aqueous NH_4Cl solution. The aqueous phase was extracted three times with *n*-pentane. The combined organic layers were dried over $MgSO_4$, filtered and the solvent was evaporated. The crude product was purified by FC (*n*-pentane) to give (1-bromoallyl)trimethylsilane (**272**) in 78% yield (30.03 g, 15.69 mmol) as colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ 5.91 (dt, *J* = 16.5, 9.8 Hz, 1H, C*H*$_{olef}$), 5.16 (dd, *J* = 16.5, 1.2 Hz, 1H, C*H*$_{olef}$), 5.03 (d, *J* = 10.0 Hz, 1H, C*H*$_{olef}$), 3.80 (d, *J* = 9.6 Hz, 1H, BrC*H*), 0.14 (s, 9H, Si(C*H*$_3$)$_3$).

^{13}C NMR (75 MHz, $CDCl_3$) δ 138.9 (*C*H$_{olef}$), 114.7 (*C*H$_{olef}$), 43.5 (Br*C*H), –1.1 (Si(*C*H$_3$)$_3$).

The NMR spectroscopic data are in accordance with the literature.[175]

(*Z*)-1-Bromo-2-(buta-1,3-dien-1-yl)benzene (273)



According to a procedure of Jiang,[130] 740 mg $CrCl_2$ were suspended in 10 mL anhydrous THF by sonication for 10 min. The slurry was cooled to 0°C before a solution of 0.7 mL 2-bromobenzaldehyde (6.0 mmol, 1.2 eq) and 966 mg (1-bromoallyl)trimethylsilane (6.0 mmol, 1.0 eq) in 10 mL anhydrous THF were added. The reaction mixture was stirred for 3 h at ambient temperature. A color change from grayish green to dark red-brown was observed. 26 mL MeOH were used to quench the reaction followed by addition of 50 mL 6 M aqueous KOH solution. The reaction was stirred overnight at ambient temperature. *n*-Pentane was then added, and the layers were separated. The slimy aqueous layer was extracted three times with *n*-pentane. The combined organic layers were dried over $MgSO_4$, filtered and the solvent was evaporated. The crude product was purified by FC (*n*-pentane) to give (*Z*)-1-bromo-2-(buta-1,3-dien-1-yl)benzene (**273**) in 54% yield (568 mg, 2.72 mmol) as colorless liquid.

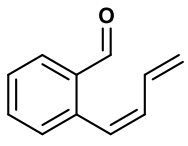
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.59 (dd, *J* = 8.0, 0.8 Hz, 1H, C*H*$_{ar}$), 7.36 (dd, *J* = 9.3, 1.6 Hz, 1H, C*H*$_{ar}$), 7.29 (dt, *J* = 8.1, 0.9 Hz, 1H, C*H*$_{ar}$), 7.13 (dt, *J* = 7.5, 1.7 Hz, 1H, C*H*$_{ar}$), 6.66 (dt, *J* = 16.9, 10.8 Hz, 1H, C*H*$_{olef}$), 6.51 (d, *J* = 11.3 Hz, 1H, C*H*$_{olef}$), 6.36 (t, *J* = 11.1 Hz, 1H, C*H*$_{olef}$), 5.41 (d, *J* = 16.8 Hz, 1H, C*H*$_{olef}$), 5.24 (d, *J* = 10.2 Hz, 1H, C*H*$_{olef}$).

^{13}C NMR (75 MHz, $CDCl_3$) δ 137.4 (*C*$_{q, ar}$), 132.9 (*C*H$_{ar}$), 132.8 (*C*H$_{ar}$), 131.9 (*C*H$_{olef}$), 131.3 (*C*H$_{olef}$), 130.0 (*C*H$_{olef}$), 128.8 (*C*H$_{ar}$), 127.1 (*C*H$_{ar}$), 124.1 (*C*$_{q, ar}$), 120.5 (*C*H$_{2, olef}$).

IR (neat) 3085, 3057, 3027, 2922, 1819, 1592, 1465, 1427, 1116, 1026, 1002, 907, 838, 812, 780, 752, 733, 695, 654.

HRMS (EI) calculated for $C_{10}H_9Br$: *m*/*z* = 207.9888; found *m*/*z* = 207.9883.

(*Z*)-2-(Buta-1,3-dien-1-yl)benzaldehyde (*Z*-262)



Under argon atmosphere, 345 mg LiCl (8.15 mmol, 3.0 eq) and 568 mg (*Z*)-1-bromo-2-(buta-1,3-dien-1-yl)benzene (2.72 mmol, 1.0 eq) were dissolved in 15 mL anhydrous THF before being cooled to −78 °C. 1.3 mL *n*-BuLi (2.5 M in *n*-hexane, 3.26 mmol, 1.2 eq) were added and the reaction mixture was stirred for 30 min at −78 °C. 15 mL ethyl formate were added and the reaction was warmed to ambient temperature.

The reaction was quenched with aqueous NH_4Cl solution and the aqueous layer was extracted three times with Et_2O. The combined organic layers were washed with brine, dried over $MgSO_4$, filtered and the solvent was evaporated. The crude product was purified by FC (*n*-pentane/Et_2O 7:1) to give (*Z*)-2-(buta-1,3-dien-1-yl)benzaldehyde (*Z*-**262**) in 49% yield (210 mg, 1.33 mmol) as colorless oil.

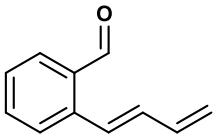
^{1}H NMR (300 MHz, $CDCl_3$) δ 10.21 (s, 1H, C*H*O), 7.90 (d, *J* = 7.8 Hz, 1H, CH_{ar}), 7.57 (dt, *J* = 7.5, 1.2 Hz, 1H, CH_{ar}), 7.43 (t, *J* = 7.5 Hz, 1H, CH_{ar}), 7.34 (d, *J* = 7.5 Hz, 1H, CH_{ar}), 6.88 (t, *J* = 10.1 Hz, 1H, CH_{olef}), 6.54 – 6.44 (m, 1H, CH_{olef}), 5.43 – 5.39 (m, 1H, CH_{olef}), 5.22 (d, *J* = 9.8 Hz, 1H, CH_{olef}).

^{13}C NMR (75 MHz, $CDCl_3$) δ 192.4 (*C*=O), 140.1 ($C_{q,\ ar}$), 133.97 (*C*H_{olef}), 133.93 (*C*H_{olef}), 133.7 (*C*H_{ar}), 132.6 ($C_{q,\ ar}$), 131.1 (*C*H_{ar}), 129.8 (*C*H_{ar}), 127.9 (*C*H_{ar}), 127.1 (*C*H_{olef}), 121.1 (*C*$H_{2,\ olef}$).

IR (neat) 2843, 2746, 1691, 1595, 1562, 1429, 1294, 1270, 1393, 1294, 1270, 1198, 1004, 910, 860, 833, 806, 758, 651, 634.

HRMS (EI) calculated for $C_{11}H_{10}O$: *m*/*z* = 158.0732; found *m*/*z* = 158.0724.

(*E*)-2-(Buta-1,3-dien-1-yl)benzaldehyde (*E*-262)



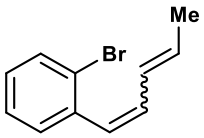
Under argon atmosphere, 194 mg magnesium turnings (8.00 mmol, 1.2 eq) were suspended in 16 mL anhydrous THF. Three drops 1,2-dibromoethane were added and the reaction was stirred at 40 °C until an exothermic reaction was observed. Then, 1.39 g (*E*)-1-bromo-2-(buta-1,3-dien-1-yl)benzene (6.67 mmol, 1.0 eq) were added and the reaction was heated to reflux overnight. After cooling the reaction mixture to 45 °C, 0.8 mL DMF (10.0 mmol, 1.5 eq) were added and the reaction mixture was stirred overnight at ambient temperature. Aqueous NH_4Cl solution was added and the aqueous layer was extracted three times with Et_2O. The combined organic layers were dried over $MgSO_4$, filtered and the solvent was evaporated. The crude product was purified by FC (*n*-pentane/Et_2O 8:1) to give (*E*)-2-(buta-1,3-dien-1-yl)benzaldehyde (***E*-262**) in 58% yield (2.02 g, 12.8 mmol) as colorless oil**.**

^{1}H NMR (300 MHz, $CDCl_3$) δ 10.27 (s, 1H, C*H*O), 7.80 (dd, *J* = 7.7, 1.1 Hz, 1H, CH_{ar}), 7.61(d, *J* = 7.6 Hz, 1H, CH_{ar}), 7.57 – 7.38 (m, 2H, CH_{ar} + CH_{olef}), 6.74 (dd, *J* = 15.4, 10.6 Hz, 1H, CH_{olef}), 6.59 (dt, *J* = 16.7, 10.1 Hz, 1H, CH_{olef}), 5.40 (d, *J* = 16.6 Hz, 1H, CH_{olef}), 5.27 (d, *J* = 10.1 Hz, 1H, CH_{olef}).

^{13}C NMR (75 MHz, $CDCl_3$) δ 192.6 (*C*=O), 139.7 ($C_{q,\,ar}$), 137.1 (CH_{olef}), 134.8 (CH_{olef}), 133.8 (CH_{ar}), 132.9 ($C_{q,\,ar}$), 132.2 (CH_{ar}), 128.6 (CH_{ar}), 127.8 (CH_{ar}), 127.1 (CH_{olef}), 119.7 ($CH_{2,\,olef}$).

The NMR spectroscopic data are in accordance with the literature.[176]

1-Bromo-2-((1*Z*,3*E*)-penta-1,3-dien-1-yl)benzene (294)



The title compound was prepared according to GP 6. First, 5.93 g *E*-crotyltriphenylphosphonium bromide (14.9 mmol, 1.2 eq) and 1.67 g potassium *tert*-butoxide (14.9 mmol, 1.2 eq) were suspended in 30 mL Et_2O at 0 °C. After stirring for 1 h at ambient temperature, 1.45 mL 2-bromobenzaldehyde (12.4 mmol, 1.0 eq) were added dropwise and the mixture was stirred overnight. Aqueous NH_4Cl solution was added and the aqueous layer was extracted three times with Et_2O. The combined organic layers were dried over $MgSO_4$, filtered, adsorbed on silica gel and the solvent was evaporated. The adsorbed crude product was purified by FC (*n*-pentane) to give 1-bromo-2-((1*Z*/*E*,3*E*)-penta-1,3-dien-1-yl)benzene (**294**) as *Z*/*E* mixture (64:36) in 68% yield (2.27 g, 10.2 mmol) as colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.51 (dd, *J* = 8.0, 1.0 Hz, 1H, C*H*$_{ar}$), 7.32 (dd, *J* = 7.6, 1.8 Hz, 1H, C*H*$_{ar}$), 7.22 (td, *J* = 7.4, 1.0 Hz, 1H, C*H*$_{ar}$), 7.00 (td, *J* = 7.5, 1.7 Hz, 1H, C*H*$_{ar}$), 6.74 – 6.54 (m, 1H, C*H*$_{olef}$), 6.33 – 6.19 (m, 2H, C*H*$_{olef}$), 5.90 – 5.79 (m, 1H, C*H*$_{olef}$), 1.70 (dd, *J* = 6.0, 1.2 Hz, 3H, C*H*$_3$).

^{13}C NMR (75 MHz, $CDCl_3$) δ 137.4 ($C_{q,\,ar}$), 133.1 (CH_{ar}), 132.2 (CH_{ar}), 131.9 (CH_{ar}), 131.8 (CH_{ar}), 128.4 (CH_{olef}), 128.3 (CH_{olef}), 127.5 (CH_{olef}), 126.4 (CH_{olef}), 123.8 ($C_{q,\,ar}$), 18.6 (CH_3).

IR (neat) 3026, 2911, 1645, 1466, 1433, 1375, 1115, 1043, 1023, 985, 943, 867, 824, 761, 739, 725, 670, 652, 621, 580.

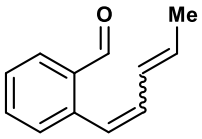
HRMS (EI) calculated for $C_{11}H_{11}Br$: *m*/*z* = 222.0044; found *m*/*z* = 222.0043.

<u>Resolved signals of the minor isomer 1-bromo-2-((1*E*,3*E*)-penta-1,3-dien-1-yl)benzene:</u>

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.46 (dt, *J* = 8.0, 1.2 Hz, 1H, C*H*$_{ar}$), 5.66 – 5.55 (m, 1H, C*H*$_{olef}$), 1.77 (dd, *J* = 7.2, 1.3 Hz, 3H, C*H*$_3$).

^{13}C NMR (75 MHz, $CDCl_3$) δ 128.6 (CH_{olef}), 126.9 (CH_{olef}), 22.5 (CH_3).

2-((1*Z*,3*E*)-Penta-1,3-dien-1-yl)benzaldehyde (274)



Under argon atmosphere, 296 mg magnesium turnings (12.2 mmol, 1.2 eq) were suspended in 30 mL anhydrous THF. Three drops 1,2-dibromoethane were added and the reaction was stirred at 40 °C until an exothermic reaction was observed. Then, 2.26 g 1-bromo-2-((1*Z*/*E*,3*E*)-penta-1,3-dien-1-yl)benzene (10.2 mmol, 1.0 eq) were added and the reaction was heated to reflux overnight. After cooling the reaction mixture to 45 °C, 1.2 mL DMF (15.2 mmol, 1.5 eq) were added and the reaction mixture was stirred overnight at ambient temperature. Aqueous NH_4Cl solution was added and the aqueous layer was extracted three times with Et_2O. The combined organic layers were dried over $MgSO_4$, filtered and the solvent was evaporated. The crude product was purified by FC (*n*-pentane/Et_2O 8:1) to give 2-((1*Z*/*E*,3*E*)-penta-1,3-dien-1-yl)benzaldehyde (**274**) as *Z*/*E* mixture (76:24) in 51% yield (887 mg, 5.16 mmol) as colorless oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 10.21 (s, 1H, C*H*O), 7.90 (dd, *J* = 7.5, 0.8 Hz, 1H, CH_{ar}), 7.56 (dt, *J* = 8.1, 1.1 Hz, 1H, CH_{ar}), 7.42 – 7.33 (m, 2H, CH_{ar}), 6.69 (d, *J* = 11.6 Hz, 1H, CH_{olef}), 6.44 (t, *J* = 11.6 Hz, 1H, CH_{olef}), 6.21 – 6.16 (m, 1H, CH_{olef}), 5.95 – 5.88 (m, 1H, CH_{olef}), 1.73 (d, *J* = 7.1 Hz, 3H, CH_3).

^{13}C NMR (125 MHz, $CDCl_3$) δ 192.5 (*C*HO), 140.8 ($C_{q, ar}$), 134.2 (*C*H_{olef}), 133.8 (*C*H_{olef}), 133.6 (*C*H_{olef}), 131.0 (*C*H_{ar}), 129.2 (*C*H_{ar}), 127.5 (*C*H_{ar}), 127.2 (*C*H_{ar}), 123.6 (*C*H_{olef}), 18.49 (*C*H_3).

IR (neat) 3026, 2930, 2854, 2730, 1724, 1693, 1645, 1595, 1561, 1479, 1447, 1392, 1292, 1269, 1196, 1159, 1068, 986, 948, 933, 863, 822, 761, 729, 702, 659, 636, 611.

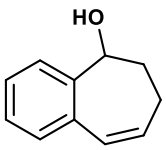
HRMS (EI) calculated for $C_{12}H_{12}O$: *m*/*z* = 172.0888; found *m*/*z* = 172.0897.

Resolved signals of the minor isomer 2-((1*E*,3*E*)-penta-1,3-dien-1-yl)benzaldehyde:

^{1}H NMR (500 MHz, $CDCl_3$) δ 10.27 (s, 1H, C*H*O), 7.78 (d, *J* = 7.6 Hz, 1H, CH_{ar}), 7.49 (t, *J* = 7.5 Hz, 1H, CH_{ar}), 6.72 (d, *J* = 15.4 Hz, 1H, CH_{olef}), 6.34 – 6.28 (m, 1H, CH_{olef}), 1.84 (d, *J* = 6.0 Hz, 3H, CH_3).

^{13}C NMR (125 MHz, $CDCl_3$) δ 192.6 (*C*HO), 132.7 (*C*H_{olef}), 134.8 (*C*H_{olef}), 131.8 (*C*H_{olef}), 129.6 (*C*H_{ar}), 127.1 (*C*H_{ar}), 126.9 (*C*H_{olef}), 125.3 (*C*H_{ar}), 18.53 (*C*H_3).

6,7-Dihydro-5*H*-benzo[7]annulen-5-ol (266)



The title compound was prepared according to GP 9 utilizing 30 mg Co(dppe)Br_2 (50 µmol, 10 mol%) and 50 mg zinc powder (0.75 mmol, 150 mol%). After 10 min, 80 mg (*Z*)-2-(buta-1,3-dien-1-yl)benzaldehyde

(0.505 mmol, 1.0 eq) were added at ambient temperature and the reaction was stirred for 24 h at ambient temperature. The crude product mixture was directly purified by FC (*n*-pentane/Et_2O 4:1) to give 6,7-dihydro-5*H*-benzo[7]annulen-5-ol (**266**) in 91% yield (72 mg, 0.460 mmol) as colorless sticky solid. The product contained 6,9-dihydro-5*H*-benzo[7]annulen-5-ol (**266'**) as by-product with an isomeric ratio **266**:**266'** of 86:14 which was determined by GC/MS and ^{1}H NMR analysis.

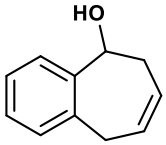
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.44 – 7.41 (m, 1H, CH_{ar}), 7.27 – 7.18 (m, 3H, CH_{ar}), 6.41 (d, *J* = 12.1 Hz, 1H, CH_{olef}), 5.95 (dt, *J* = 12.1, 4.6 Hz, 1H, CH_{olef}), 4.89 (d, *J* = 7.2 Hz, 1H, C*H*), 2.57 – 2.47 (m, 2H, CH_2), 2.27 – 2.08 (m, 2H, CH_2), 1.96 (s, 1H, O*H*).

^{13}C NMR (75 MHz, $CDCl_3$) δ 142.7 ($C_{q, ar}$), 134.2 ($C_{q, ar}$), 131.6 (CH$_{olef}$), 131.6 (CH$_{ar}$), 129.5 (CH$_{olef}$), 127.5 (CH$_{ar}$), 126.9 (CH$_{ar}$), 126.7 (CH$_{ar}$), 73.5 (*C*H), 34.0 (CH$_2$), 26.9 (CH$_2$).

IR (neat) 3356, 3017, 2926, 2891, 1657, 1485, 1448, 1425, 1342, 1289, 1255, 1199, 1174, 1107, 1044, 781, 763, 731, 655.

HRMS (EI) calculated for $C_{11}H_{12}O$: *m*/*z* = 160.0883; found *m*/*z* = 160.0875.

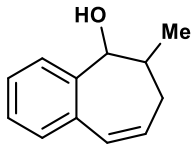
Resolved signals of the minor isomer 6,9-dihydro-5*H*-benzo[7]annulen-5-ol:



^{1}H NMR (300 MHz, $CDCl_3$) δ 7.48 (d, *J* = 7.5 Hz, 1H, CH_{ar}), 7.08 (d, *J* = 7.4 Hz, 1H, CH_{ar}), 5.81 – 5.73 (m, 1H, CH_{olef}), 5.55 – 5.48 (m, 1H, CH_{olef}), 5.36 (d, *J* = 11.1 Hz, C*H*), 3.64 (dt, *J* = 17.1, 3.2 Hz, 1H, CH_2), 3.27 (dd, *J* = 16.9, 7.3 Hz, 1H, CH_2), 2.71 – 2.65 (m, 1H, CH_2), 2.44 – 2.32 (m, 1H, CH_2), 1.98 (s, 1H, O*H*).

^{13}C NMR (75 MHz, $CDCl_3$) δ 143.4 ($C_{q, ar}$), 138.7 ($C_{q, ar}$), 132.6 (CH$_{ar}$), 128.3 (CH$_{ar}$), 127.1 (CH$_{ar}$), 126.1 (CH$_{olef}$), 123.8 (CH$_{olef}$), 70.5 (*C*H), 38.1 (CH$_2$), 33.7 (CH$_2$).

6-Methyl-6,7-dihydro-5*H*-benzo[7]annulen-5-ol (275) and 6-Methyl-6,9-dihydro-5*H*-benzo[7]annulen-5-ol (275')



The title compound was prepared according to GP 9 utilizing 30 mg Co(dppe)Br_2 (50 μmol, 10 mol%) and 50 mg zinc powder (0.75 mmol, 150 mol%). After 10 min, 86 mg 2-((1*Z*,3*E*)-penta-1,3-dien-1-yl)benzaldehyde (0.500 mmol, 1.0 eq) were added at ambient temperature and the reaction was stirred for 24 h at ambient temperature. The crude product mixture was directly purified by FC (*n*-pentane/Et_2O 4:1) to give 6-methyl-6,7-dihydro-5*H*-benzo[7]annulen-5-ol (**275**) in 40% yield (34 mg, 0.105 mmol) as colorless oil. The product contained 6-methyl-6,9-dihydro-5*H*-

benzo[7]annulen-5-ol (**275'**) as by-product with an isomeric ratio **275**:**275'** of 74:26 which was determined by GC/MS and ^{1}H NMR analysis.

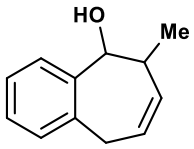
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.41 – 7.38 (m, 1H, CH_{ar}), 7.34 – 7.23 (m, 3H, CH_{ar}), 6.46 (d, *J* = 12.0 Hz, 1H, CH_{olef}), 5.94 (dt, *J* = 12.2, 5.1 Hz, 1H, CH_{olef}), 4.74 (d, *J* = 3.8 Hz, 1H, C*H*), 2.53 – 2.36 (m, 3H, C*H* + CH_2), 1.92 (d, *J* = 5.0 Hz, 1H, O*H*), 1.11 (d, *J* = 6.3 Hz, 3H, CH_3).

^{13}C NMR (75 MHz, $CDCl_3$) δ 141.4 ($C_{q, ar}$), 135.6 ($C_{q, ar}$), 134.6 (*C*H$_{ar}$), 131.5 (*C*H$_{olef}$), 129.1 (*C*H$_{olef}$), 128.5 (*C*H$_{ar}$), 127.7 (*C*H$_{ar}$), 127.0 (*C*H$_{ar}$), 78.7 (*C*H), 37.1 (*C*H), 34.5 (*C*H$_2$), 19.3 (*C*H$_3$).

IR (neat) 3393, 3015, 2958, 2883, 1449, 1422, 1243, 1032, 971, 947, 776, 753, 708, 609, 570.

HRMS (ESI) calculated for $C_{12}H_{14}OLi^+$: *m*/*z* = 181.1205; found *m*/*z* = 181.1203.

Resolved signals of the minor isomer 6-methyl-6,9-dihydro-5*H*-benzo[7]annulen-5-ol:

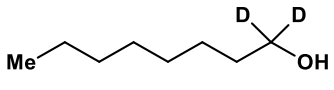


^{1}H NMR (300 MHz, $CDCl_3$) δ 7.43 – 7.41 (d, *J* = 7.3 Hz, 1H, CH_{ar}), 5.75 – 5.69 (m, 1H, CH_{olef}), 5.47 – 5.41 (m, 1H, CH_{olef}), 3.60 (dq, *J* = 17.0, 2.5 Hz, 1H, C*H*), 3.24 (dd, *J* = 16.9, 7.1 Hz, 1H, CH_2), 0.85 (d, *J* = 7.1 Hz, 3H, CH_3).

^{13}C NMR (75 MHz, $CDCl_3$) δ 141.1 ($C_{q, ar}$), 135.7 ($C_{q, ar}$), 131.2 (*C*H$_{ar}$), 130.7 (*C*H$_{olef}$), 130.0 (*C*H$_{olef}$), 129.7 (*C*H$_{ar}$), 127.6 (*C*H$_{ar}$), 39.5 (*C*H), 32.8 (*C*H$_2$), 17.6 (*C*H$_3$).

5.7 Synthesis of Deuterated Compounds

Octan-1,1-*d*$_2$-1-ol (295-*d*$_2$)



590 mg lithium aluminum deuteride (14.0 mmol, 2.0 eq) were suspended in 100 mL anhydrous THF and 1.11 g ethyl octanoate (7.00 mmol, 1.0 eq) were added at 0 °C. The reaction mixture was stirred for 1 h at ambient temperature. It was then quenched with 0.6 mL water, 0.6 mL aqueous NaOH (15 w-%) and 0.2 mL water. The mixture was filtered, the precipitate was rinsed thoroughly with Et_2O and the filtrate was evaporated to give octan-1,1-*d*$_2$-1-ol (**295**-*d*$_2$) in 96% yield (890 mg, 6.73 mmol) as colorless oil and quantitative deuterium incorporation.

^{1}H NMR (300 MHz, $CDCl_3$) δ 1.55 (d, *J* = 6.9 Hz, 2H, C*H*$_2$), 1.36 – 1.20 (m, 11H, C*H*$_2$ + O*H*), 0.88 (t, *J* = 6.9 Hz, 3H, C*H*$_3$).

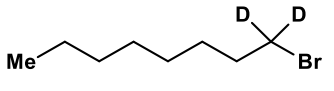
^{2}H NMR (46 MHz, $CHCl_3$) δ 3.41 (s, 2D, C*D*$_2$OH).

^{13}C NMR (75 MHz, $CDCl_3$) δ 32.8 (*C*H_2), 32.0 (*C*H_2), 29.5 (*C*H_2), 29.4 (*C*H_2), 25.9 (*C*H_2), 22.8 (*C*H_2), 14.2 (*C*H_3). *C*D_2OH not detectable.

IR (neat) 3333, 2956, 2924, 2854, 2190, 2093, 1464, 1378, 1296, 1185, 1131, 1091, 1073, 967, 907, 722, 650.

HRMS (EI) calculated for $C_8H_{15}D_2$: *m*/*z* = 114.1456; found *m*/*z* = 114.3774.

1-Bromooctane-1,1-*d*$_2$ (296-*d*$_2$)



Under argon atmosphere, 890 mg octan-1,1-*d*$_2$-1-ol (6.73 mmol, 1.0 eq) and 3.55 g CBr_4 (10.1 mmol, 1.5 eq) were dissolved in 20 mL anhydrous dichloromethane. Then, 2.65 g PPh_3 (10.1 mmol, 1.5 eq) were added in three portions. The reaction mixture was stirred at ambient temperature for 1 h. Another 1.5 eq of PPh_3 were added and the mixture was stirred for another hour. The crude product mixture was adsorbed on silica. After purification by FC (*n*-pentane) 1-bromooctane-1,1-*d*$_2$ (**296**-*d*$_2$) was obtained in 76% yield (997 mg, 5.11 mmol) as colorless oil and quantitative deuterium incorporation.

^{1}H NMR (300 MHz, $CDCl_3$) δ 1.84 (t, *J* = 7.9 Hz, 2H, C*H*$_2$), 1.46 – 1.38 (m, 2H, C*H*$_2$), 1.37 – 1.28 (m, 8H, C*H*$_2$), 0.89 (t, *J* = 7.2 Hz, 3H, C*H*$_3$).

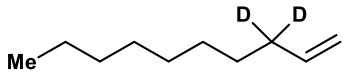
^{2}H NMR (46 MHz, $CHCl_3$) δ 3.18 (s, 2D, C*D*$_2$OH).

^{13}C NMR (75 MHz, $CDCl_3$) δ 32.8 (*C*H_2), 31.9 (*C*H_2), 29.3 (*C*H_2), 28.9 (*C*H_2), 28.3 (*C*H_2), 22.8 (*C*H_2), 14.2 (*C*H_3).*C*D_2Br not detectable.

IR (neat) 2955, 2924, 2855, 2156, 1464, 1378, 1115, 993, 957, 927, 911, 723, 675, 607, 541.

HRMS (EI) calculated for $C_8H_{15}D_2Br$: *m*/*z* = 194.06392; found *m*/*z* = 194.06347.

Dec-1-ene-3,3-*d*$_2$ (297-*d*$_2$)



According to a procedure of Oshima,[177] 111 mg Ni(dppp)Cl_2 (205 μm, 10 mol%) and 220 mg vinylbromide (2.05 mmol, 1.0 eq) were dissolved in anhydrous THF under argon atmosphere. In a second flask under argon atmosphere, 60 mg magnesium turnings (2.46 mmol, 1.2 eq) and 400 mg bromooctane-1,1-*d*$_2$ (2.05 mmol, 1.0 eq) were suspended in anhydrous THF and stirred for 5 h at ambient temperature. The Grignard solution was then transferred into the first flask containing the nickel catalyst and vinylbromide. The reaction was stirred for 5 h at 35 °C. It was filtered through a short pad of silica. After purification by vacuum distillation (15 mbar, 67 °C) dec-1-ene-3,3-*d*$_2$ (**297**-*d*$_2$) was obtained in 46% yield (132 mg, 0.93 mmol) as colorless oil and quantitative deuterium incorporation. As byproduct hexadecane-8,8,9,9-*d*$_4$ was obtained in 45% yield (216 mg, 0.93 mmol).

^{1}H NMR (300 MHz, $CDCl_3$) δ 5.80 (dd, *J* = 17.1, 10.2 Hz, 1H, C*H*$_{olef}$), 4.98 (dd, *J* = 17.1, 2.2 Hz, 1H, C*H*$_{2,\ olef}$), 4.92 (dd, *J* = 10.2, 2.2 Hz, 1H, C*H*$_{2,\ olef}$), 1.27 (br s, 12H, C*H*$_2$), 0.88 (t, *J* = 7.1 Hz, 3H, C*H*$_3$).

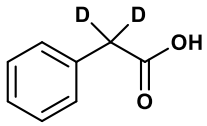
^{2}H NMR (46 MHz, $CHCl_3$) δ 1.82 (s, 2D, C*D*$_2$OH).

^{13}C NMR (75 MHz, $CDCl_3$) δ 139.4 (*C*H$_{olef}$), 114.3 (*C*H$_{2,\ olef}$), 34.3 (*C*H_2), 32.1 (*C*H_2), 29.6 (*C*H_2), 29.4 (*C*H_2), 29.3 (*C*H_2), 29.0 (*C*H_2), 22.8 (*C*D_2), 14.2 (*C*H_3).

IR (neat) 2958, 2922, 2854, 2180, 2092, 1673, 1465, 1412, 1377, 1339, 1260, 1146, 1059, 993, 967, 909, 845, 722.

HRMS (EI) calculated for $C_{10}H_{18}D_2$: *m*/*z* = 142.16905; found *m*/*z* = 142.16886.

2-Phenylacetic-2,2-*d*$_2$ acid (298-*d*$_2$)



According to a procedure of Gao,[23] 5.44 g phenylacetic acid (40 mmol, 1.0 eq) were dissolved in 10 mL of a solution containing 40 w-% NaOD in deuterium oxide (97.6 mmol, 2.3 eq). The reaction mixture was heated for 12 h to 100 °C, was then cooled to ambient temperature and acidified with 2 M aqueous HCl to

pH 2. The aqueous layer was extracted three times with dichloromethane, the organic layer was dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure to give 2-phenylacetic-2,2-d_2 acid (**298**-d_2) in quantitative yield (5.52 g, 39.9 mmol) as a white solid and 95% deuterium incorporation.

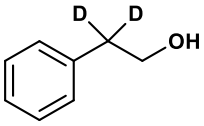
^{1}H NMR (300 MHz, $CDCl_3$) δ 11,79 (br s, 1H, COO*H*), 7.37 – 7.28 (m, 5H, CH_{ar}).

^{2}H NMR (77 MHz, $CHCl_3$) δ 3.65 (s, 2D, CD_2).

^{13}C NMR (75 MHz, $CDCl_3$) δ 178.3 (*C*OOH), 133.3 ($C_{q, ar}$), 129.5 (CH_{ar}), 128.8 (CH_{ar}), 127.5 (CH_{ar}), 40.7 (quin, *J* = 19.7 Hz, *C*D_2).

The NMR spectroscopic data are in accordance with the literature.[23]

2-Phenylethan-2,2-d_2-1-ol (299-d_2)



According to a procedure of Gao,[23] under argon atmosphere, 1.23 g lithium aluminum hydride (32.6 mmol, 1.5 eq) in 40 mL anhydrous was added dropwise 3.00 g phenylacetic-2,2-d_2 acid (21.7 mmol, 1.0 eq) in 40 mL anhydrous THF. The reaction mixture was stirred 1 h at ambient temperature. It was then quenched with 0.5 M aqueous HCl. The mixture was filtered, and the precipitate was thoroughly rinsed with EtOAc. The organic layer was washed with water and brine, dried over $MgSO_4$, and the solvent was evaporated. After purification by FC (*n*-pentane/Et_2O 4:1) 2-phenylethan-2,2-d_2-1-ol (**299**-d_2) was obtained in 99% yield (2.67 g, 21.5 mmol) as colorless oil and 95% deuterium incorporation.

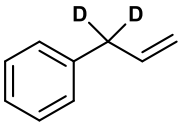
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.34 (t, *J* = 7.8 Hz, 2H, CH_{ar}), 7.28 – 7.24 (m, 3H, CH_{ar}), 3.87 (d, *J* = 6.0 Hz, 2H, CH_2OH), 1.68 (br s, 1H, O*H*).

^{2}H NMR (77 MHz, $CHCl_3$) δ 4.29 (s, 2D, CD_2).

^{13}C NMR (75 MHz, $CDCl_3$) δ 138.6 ($C_{q, ar}$), 129.1 (CH_{ar}), 128.7 (CH_{ar}), 126.5 (CH_{ar}), 60.5 (*C*H_2OH), 38.8 (quin, *J* = 19.1 Hz, *C*D_2).

The NMR spectroscopic data are in accordance with the literature.[23]

(Allyl-1,1-d_2)benzene (17-d_2)



According to a procedure of Gao,[23] 1.60 g pyridinium chlorochromate (7.50 mmol, 1.5 eq) and 7.5 g silica were suspended in 15 mL anhydrous dichloromethane and 0.62 g 2-phenylethan-2,2-d_2-1-ol (5.00 mmol, 1.0 eq) in

10 mL anhydrous dichloromethane were added. The reaction mixture was stirred 5 h at ambient temperature. The mixture was filtered through a short pad of silica gel and the precipitate was washed with Et_2O. The solvent was evaporated. The aldehyde was then used for a subsequent Wittig reaction following the standard protocol of GP 6. After purification by FC (*n*-pentane) (allyl-1,1-d_2)benzene (**17**-d_2) was obtained in 37% yield (220 mg, 1.83 mmol) as colorless liquid and 88% deuterium incorporation.

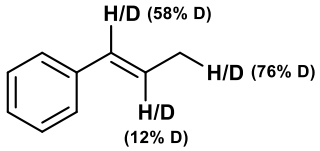
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.32 – 7.18 (m, 5H, CH_{ar}), 6.02 – 5.92 (m, 1H, CH_{olef}), 5.11 – 5.06 (m, 2H, C$H_{2,\ olef}$), 3.39 (br s, 0.24 H, CH_2).

^{2}H NMR (77 MHz, $CHCl_3$) δ 3.40 (s, 1D, CD_2).

^{13}C NMR (75 MHz, $CDCl_3$) δ 137.5 (*C*H_{olef}), 128.7 (*C*H_{ar}), 128.6 (*C*H_{ar}), 126.2 (*C*H_{ar}), 115.9 (*C*$H_{2,\ olef}$). $C_{q,\ ar}$ and *C*D_2 not detectable.

The NMR spectroscopic data are in accordance with the literature.[23]

(*E*)-(Prop-1-en-1-yl-1,2,3-d_3)benzene (18-*d*)



The title compound was prepared according to a modified GP 1 utilizing 31 mg Ni(dppp)Br_2 (50.0 µmol, 10 mol%), 6.6 mg zinc powder (100 µmol, 20 mol%), 32.0 mg zinc iodide (100 µmol, 20 mol%) in 0.25 mL anhydrous dichloromethane. Note, that diphenylphosphine was NOT used! 60 mg (allyl-1,1-d_2)benzene (0.25 mmol, 1.0 eq) were added after 10 min. The reaction mixture was stirred 24 h at ambient temperature. After general workup (*E*)-(prop-1-en-1-yl-1,2,3-d_3)benzene (**18**-*d*) was obtained in 68% yield (41.0 mg, 0.341 mmol) as colorless oil and 58% remaining deuterium at position 1, 12% deuterium incorporation at position 2, and 76% deuterium incorporation at position 3.

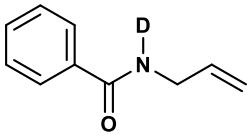
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35 – 7.29 (m, 4H, CH_{ar}), 7.22 – 7.17 (m, 1H, CH_{ar}), 6.42 (d, *J* = 15.9 Hz, 0.42 H, CH_{olef}), 6.32 – 6.20 (m, 0.88 H, CH_{olef}), 1.88 (d, *J* = 6.3 Hz, 2.24 H, CH_2D).

^{2}H NMR (77 MHz, $CHCl_3$) δ 6.46 (br s, 1D, CD_{olef}), 6.30 (br s, 0.24 D, CD_{olef}), 1.92 (br s, 1.28 D, CH_2D).

^{13}C NMR (75 MHz, $CDCl_3$) δ 138.1 (d, *J* = 4.9 Hz, $C_{q,\ ar}$), 131.2 (*C*H_{olef}), 128.6 (*C*H_{ar}), 126.9 (*C*H_{ar}), 125.9 (*C*H_{ar}), 125.8 (d, *J* = 8.9 Hz, *C*H_{olef}), 18.6 (br s, *C*H_2D).

The NMR spectroscopic data are in accordance with the literature.[23]

***N*-Allyl-*N*-*d*-benzamide (72e-*d*)**



Under argon atmosphere, 386 mg *N*-allylbenzamide (2.40 mmol, 1.0 eq) were dissolved in 5.0 mL ahydrous THF and cooled to −78 °C. 1.5 mL *n*-BuLi (1.6 M in *n*-hexane, 2.40 mmol, 1.0 eq) were added and the reaction mixture was stirred for 1 h at −78 °C. The reaction was quenched with 0.1 mL D_2O (4.80 mmol, 2.0 eq) and the aqueous layer was extracted with EtOAc, dried over Na_2SO_4, filtered and the solvent was evaporated to give *deutero*-*N*-allylbenzamide (**72e**-*d*) in 69% yield (296 mg, 1.66 mmol) as colorless oil.

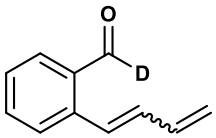
^{1}H NMR (300 MHz, DMSO-d_6) δ 7.90 – 7.85 (m, 2H, CH_{ar}), 7.56 – 7.43 (m, 3H, CH_{ar}), 5.96 – 5.83 (m, 1H, CH_{olef}), 5.17 (dq, *J* = 15.4, 1.8 Hz, 1H, CH_{olef}), 5.07 (dq, *J* = 10.2, 1.7 Hz, 1H, CH_{olef}), 3.89 (dt, *J* = 5.1, 1.6 Hz, 2H, CH_2).
^{2}H NMR (46 MHz, DMSO) δ 8.95 (br s, N*D*).

^{13}C NMR (75 MHz, $CDCl_3$) δ 167.5 (*C*=O), 134.7 ($C_{q, ar}$), 134.3 (*C*H_{olef}), 131.6 (*C*H_{ar}), 128.7 (*C*H_{ar}), 127.1 (*C*H_{ar}), 116.8 (*C*$H_{2, olef}$), 42.6 (*C*H_2).

IR (neat) 3064, 2917, 2476, 1626, 1577, 1451, 1437, 1412, 1274, 1186, 1158, 1141, 1075, 989, 946, 917, 845, 800, 707, 690, 668, 631, 617, 547, 494.

HRMS (ESI) calculated for $C_{10}H_{10}ODNa^+$: *m*/*z* = 185.0734; found *m*/*z* = 185.0767.

***Deutero*-(*Z*/*E*)-2-(Buta-1,3-dien-1-yl)benzaldehyde (262-*d*)**



Under argon atmosphere, 0.70 g 1-bromo-2-(buta-1,3-dienyl)benzene (3.30 mmol, 1.0 eq) and 420 mg LiCl (9.90 mmol, 3.0 eq) were suspended in 20 mL anhydrous THF and cooled to −78 °C. 2.5 mL *n*-BuLi (1.6 M in *n*-hexane, 4.00 mmol, 1.2 eq) were added and the reaction was stirred for 30 min at −78 °C. Then, 0.76 mL DMF-d_7 (9.90 mmol, 3.0 eq) were added and the reaction was stirred for another 15 min. It was then quenched with aqueous NH_4Cl. The aqueous layer was extracted three times with Et_2O. The organic layer was dried over $MgSO_4$, filtered and the solvent was evaporated to give *deutero*-(*Z*/*E*)-2-(buta-1,3-dien-1-yl)benzaldehyde (**262**-*d*) as *Z*/*E* mixture (86:14) as a colorless oil. The product was used without further purification.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.89 (dd, *J* = 7.8, 0.9 Hz, 1H, CH_{ar}), 7.55 (dt, *J* = 7.5, 1.2 Hz, 1H, CH_{ar}), 7.41 (t, *J* = 7.6 Hz, 1H, CH_{ar}), 7.32 (d, *J* = 7.6 Hz, 1H, CH_{ar}), 6.86 (d, *J* = 10.4 Hz, 1H, CH_{olef}), 6.50 – 6.43 (m, 2H, CH_{olef}), 5.41 – 5.38 (m, 1H, CH_{olef}), 5.21 (d, *J* = 9.7 Hz, 1H, CH_{olef}).

^{2}H NMR (77 MHz, $CHCl_3$) δ 10.24 (s, 1D, C*D*O).

^{13}C NMR (125 MHz, $CDCl_3$) δ 191.9 (t, *J* = 27.2 Hz, D*C*=O), 140.0 ($C_{q,\ ar}$), 133.9 (CH_{olef}), 133.6 (CH_{ar}), 132.0 ($C_{q,\ ar}$), 132.5 (CH_{olef}), 131.0 (CH_{ar}), 129.6 (CH_{ar}), 127.75 (CH_{ar}), 127.0 (CH_{olef}), 121.0 ($CH_{2,\ olef}$).

IR (neat) 2928, 2111, 1675, 1649, 1598, 1563, 1431, 1213, 1006, 911, 797, 756, 702, 647.

HRMS (ESI) calculated for $C_{11}H_9ODLi^+$: *m*/*z* = 166.0954; found *m*/*z* = 166.0959.

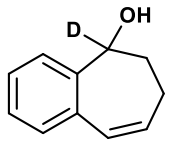
Resolved signals of the minor isomer *deutero*-(*E*)-2-(buta-1,3-dien-1-yl)benzaldehyde:

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.80 (d, *J* = 8.7 Hz, 1H, C*H*$_{ar}$), 7.60 (d, *J* = 8.1 Hz, 1H, C*H*$_{ar}$), 6.62 – 6.53 (m, 2H, C*H*$_{olef}$).

^{2}H NMR (77 MHz, $CHCl_3$) δ 10.30 (s, 1D, C*D*O).

^{13}C NMR (125 MHz, $CDCl_3$) δ 139.7 ($C_{q,\ ar}$), 134.7 (CH_{olef}), 133.2 (CH_{ar}), 130.8 (CH_{ar}), 130.4 (CH_{ar}), 127.69 (CH_{ar}), 127.1 (CH_{olef}), 119.7 ($CH_{2,\ olef}$).

6,7-Dihydro-5*H*-benzo[7]annulen-5-*d*-5-ol (266-*d*)



The title compound was prepared according to GP 9 utilizing 30 mg Co(dppe)Br_2 (50 μmol, 10 mol%) and 50 mg zinc powder (0.75 mmol, 150 mol%). After 10 min, 80 mg *deutero*-(*Z*)-2-(buta-1,3-dien-1-yl)benzaldehyde (0.505 mmol, 1.0 eq) were added at ambient temperature and the reaction was stirred for 24 h at ambient temperature. The crude product mixture was directly purified by FC (*n*-pentane/Et_2O 4:1) to give 6,7-dihydro-5*H*-benzo[7]annulen-5-*d*-5-ol (**266**-*d*) in 54% yield (43 mg, 0.273 mmol) as colorless sticky solid. The product contained and 6,9-dihydro-5*H*-benzo[7]annulen-5-*d*-5-ol (**266'**-*d*) as by-product with an isomeric ratio **266**-*d*:**266'**-*d* of 85:15 which was determined by GC/MS and ^{1}H NMR analysis.

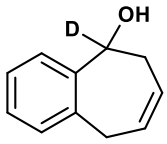
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.43 – 7.42 (m, 1H, C*H*$_{ar}$), 7.28 – 7.18 (m, 3H, C*H*$_{ar}$), 6.41 (d, *J* = 12.1 Hz, 1H, C*H*$_{olef}$), 5.94 (dt, *J* = 12.1, 4.6 Hz, 1H, C*H*$_{olef}$), 2.61 – 2.52 (m, 1H, C*H*$_2$), 2.50 – 2.43 (m, 1H, C*H*$_2$), 2.23 – 2.17 (m, 1H, C*H*$_2$), 2.12 – 2.08 (m, 1H, C*H*$_2$), 1.91 (s, 1H, O*H*).
^{2}H NMR (77 MHz, $CHCl_3$) δ 4.90 (s, 1D, C*D*OH).

^{13}C NMR (125 MHz, $CDCl_3$) δ 142.7 ($C_{q,\ ar}$), 134.3 ($C_{q,\ ar}$), 132.6 (CH_{olef}), 131.6 (CH_{ar}), 129.5 (CH_{olef}), 127.5 (CH_{ar}), 127.0 (CH_{ar}), 126.8 (CH_{ar}), 72.9 (t, *J* = 44.2 Hz, *C*DOH), 33.9 (CH_2), 26.8 (CH_2).

IR (neat) 3373, 2926, 1659, 1446, 1255, 1117, 1078, 1060, 947, 908, 778, 762, 730, 575.

HRMS (ESI) calculated for $C_{11}H_{12}ONa^+$: *m*/*z* = 184.0849; found *m*/*z* = 184.1004.

Resolved signals of the minor isomer 6,9-dihydro-5*H*-benzo[7]annulen-5-*d*-5-ol:



^{1}H NMR (500 MHz, $CDCl_3$) δ 7.48 (d, *J* = 7.5 Hz, 1H, C*H*$_{ar}$), 7.08 (d, *J* = 7.4 Hz, 1H, C*H*$_{ar}$), 5.80 – 5.71 (m, 1H, C*H*$_{olef}$), 5.58 – 5.49 (m, 1H, C*H*$_{olef}$), 3.27 (m, 1H, C*H*$_2$), 2.70 – 2.66 (m, 1H, C*H*$_2$), 2.01 (s, 1H, O*H*).

^{13}C NMR (125 MHz, $CDCl_3$) δ 128.3 (*C*H$_{ar}$), 127.1 (*C*H$_{ar}$), 126.1 (*C*H$_{olef}$), 123.8 (*C*H$_{olef}$), 33.7 (*C*H$_2$).

5.8 Abbreviations

Å	Ångström
Ac	acetyl
acac	acetyl acetonate
Alk	alkyl
Ar	aryl
atm	atmospheric pressure
BARF	tetrakis[3,5-bis(trifluoromethyl)-phenyl]borate
bdpp	pentane-2,4-diylbis(biphenyl-λ^4-phosphine)
BINAP	2,2′-bis(diphenylphosphino)-1,1′-binaphthyl
B.O.	bond order (German: *Bindungsordnung*)
Boc	*tert*-butoxy carbamate
Bn	benzyl
Bu	butyl
BuLi	butyllithium
Cbz	Carboxybenzyl
cf.	compare
cod	cyclooctadiene
CV	cyclic voltammetry
Cy	cyclohexyl
d	dublet, day
δ	delta, chemical shift
dArpp	pentane-2,4-diylbis(bis(4-methoxyphenyl)-λ^4-phosphine)
DCE	1,2-dichloroethane
de	diasteremeric excess
DFT	density functional theory
DIBAL	di*iso*butyl aluminum hydride
DMAP	4-dimethylaminopyridine
DMB	2,3-dimethylbuta-1,3-diene
DME	dimethoxyethane
DMF	*N*,*N*-dimethyl formamide
DMPU	1,3-dimethyl-3,4,5,6-tetrahydro-2(1*H*)-pyrimidinone
DMSO	dimethylsulfoxide

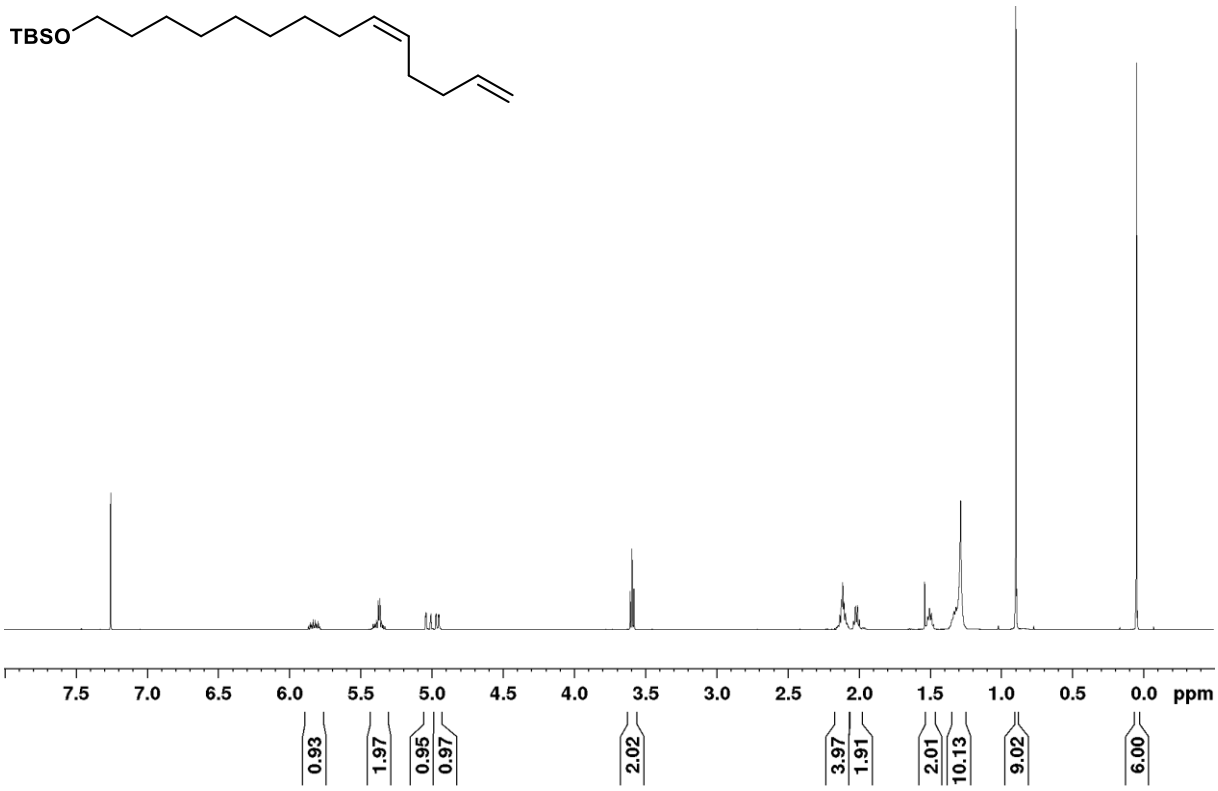
d(*o*-Tol)pp	1,3-bis(di-*o*-tolylphosphinyl)propane
dppb	1,2-bis(diphenylphosphino)butane
dppe	1,2-bis(diphenylphosphino)ethane
dppm	1,2-bis(diphenylphosphino)methane
dppp	1,2-bis(diphenylphosphino)propane
dpppBuEt	(2-butyl-2-ethylpropane-1,3-di-yl)bis(biphenyl-λ^4-phosphine)
dpppMe$_2$	(2,2-dimethylpropane-1,3-diyl)bis(biphenyl-λ^4-phosphine)
d.r.	diastereomeric ratio
E	energy
$E_{1/2}$	half-wave potential
ee	enantiomeric excess
EI	electron impact ionization
EPR	electron paramagnetic resonance
eq	equivalents
equat.	equatorial
e.r.	enatiomeric ratio
ESI	electron spray ionization
EWG	electron withdrawing group
FC	flash column chromatography
Fc/Fc$^+$	ferrocene/ferrocenium
FG	functional group
FID	flame ionization detector
FT	Fourier transform
GC	gas chromatograph(y)
GC/MS	gas chromatograph coupled with a mass-selective detector
GP	general procedure
h	hour
HAT	hydrogen atom transfer
HPLC	high performance liquid chromatography
HRMS	high resolution mass spectrometry
HV	high vacuum
Hz	Hertz
I	current, nuclear spin
ie	isomeric excess

IMes	1,3-bis(2,4,6-trimethylphenyl)imidazole
i.r.	isomeric ratio
IR	infrared
IS	internal standard
J	coupling constant
JvW	Jacobi von Wangelin
K	Kelvin
KR	kinetic resolution
L	ligand
LG	leaving group
m	*meta*
M	molar
[M]	metal complex
Me-DuPHOS	(−)-1,2-bis[(2*R*,5*R*)-2,5-dimethylphospholano]benzene
Mes	mesityl
min	minute
MS	mass-selective detector
MTBE	methyl *tert*-butyl ether
m/z	mass-to-charge ratio
ν	wavenumber
n.d.	not detectable
n.i.	not isolated
NMR	nuclear magnetic resonance
o	*ortho*
o/n	overnight
p	*para*
PCC	pyridinium chlorochromate
PG	protecting group
Ph	phenyl
pin	pinacolyl
ppm	part per million
Pr	propyl
py-imin	(*E*)-2-((pyridin-2-ylmethylene)-amino)ethan-1-amine
R	rest

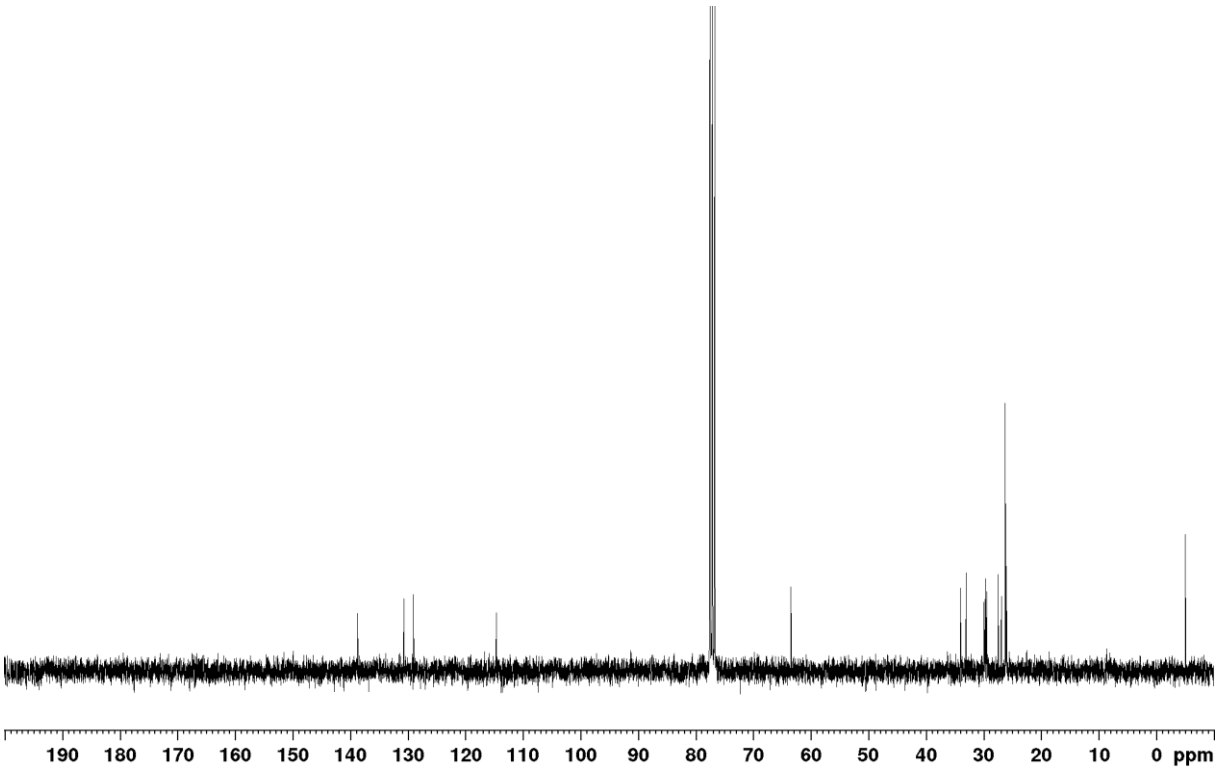
®	registered trademark
RCM	ring closing metathesis
r.r.	regioisomeric ratio
rt	room (ambient) temperature
sal$^{t\text{Bu}/t\text{Bu}}$	(*R,R*)-(−)-*N,N′*-Bis(3,5-di-*tert*-butylsalicylidene)-1,2-cyclohexanediamin
SHOP	Shell Higher Olefin Process
s.m.	starting material
t	tertiary, time
T	temperature
TBA	tetrabutylammonium
TBS	*tert*-butyl dimethyl silyl
Tf	triflyl
THF	tetrahydrofuran
TLC	thin layer chromatography
TMEDA	tetramethyl ethylene diamine
TMS	trimethylsilyl
Tol	tolyl
Tos	tosyl
(*R*)-TRIP	(*R*)-3,3′-bis(2,4,6tri*iso*propyl-phen-yl)-1,1′-binaphthyl-2,2′-diyl hydrogenphosphate
TS	transition state
u	unit ($^{kg}/_{C}$ for m/z)
üN	overnight; German: *über Nacht*
ZPE	zero-point energy

5.9 NMR Spectra of Selected Compounds

(*Z*)-*tert*-Butyldimethyl(tetradeca-9,13-dien-1-yloxy)silane (185)

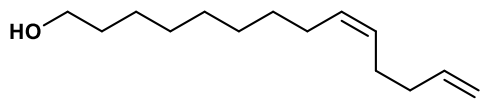


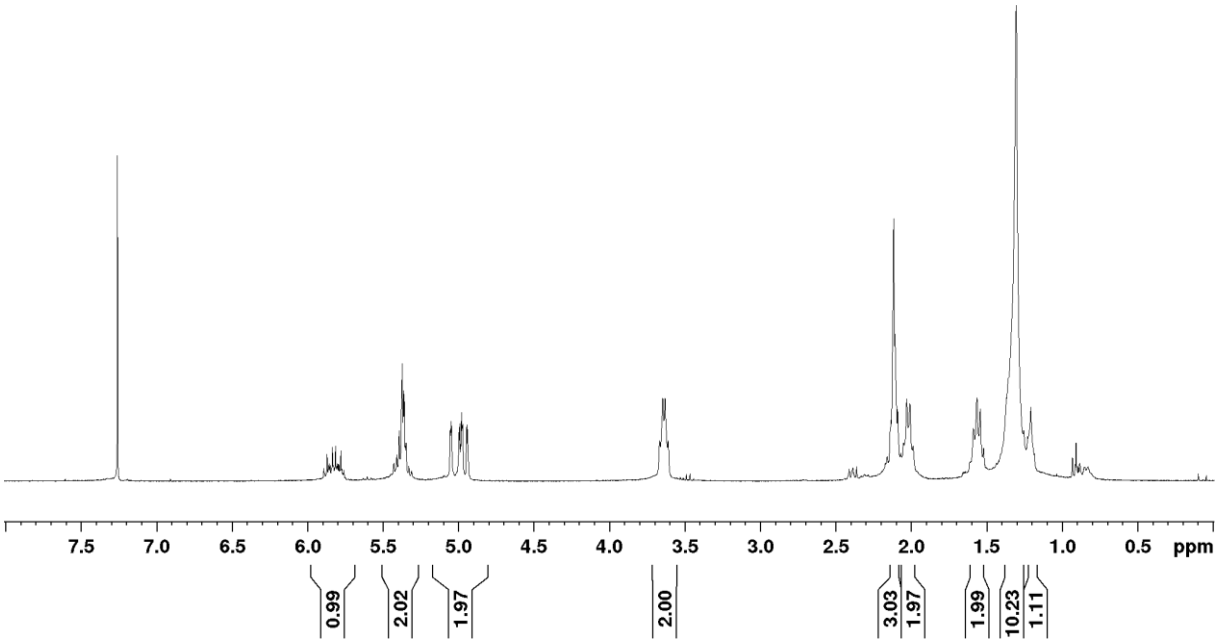
^{1}H NMR (500 MHz, $CDCl_3$).



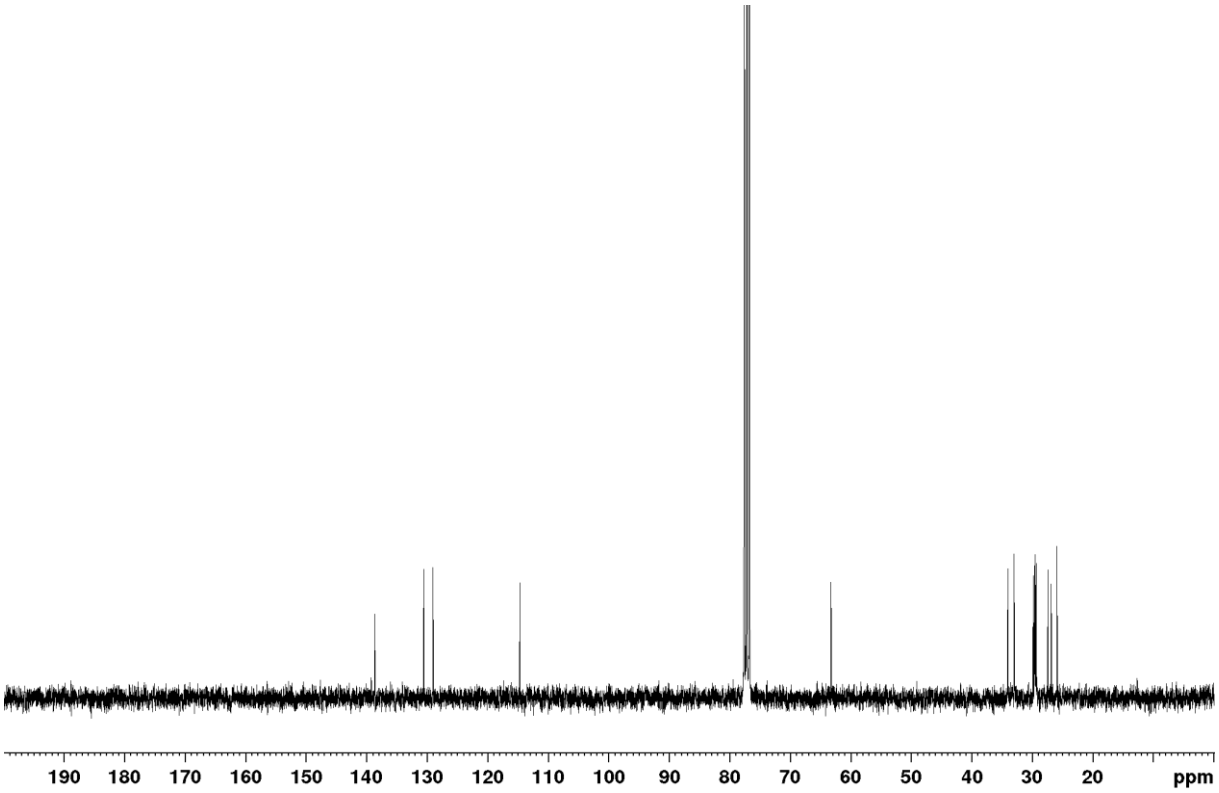
^{13}C NMR (75 MHz, $CDCl_3$).

(*Z*)-Tetradeca-9,13-dien-1-ol (284)



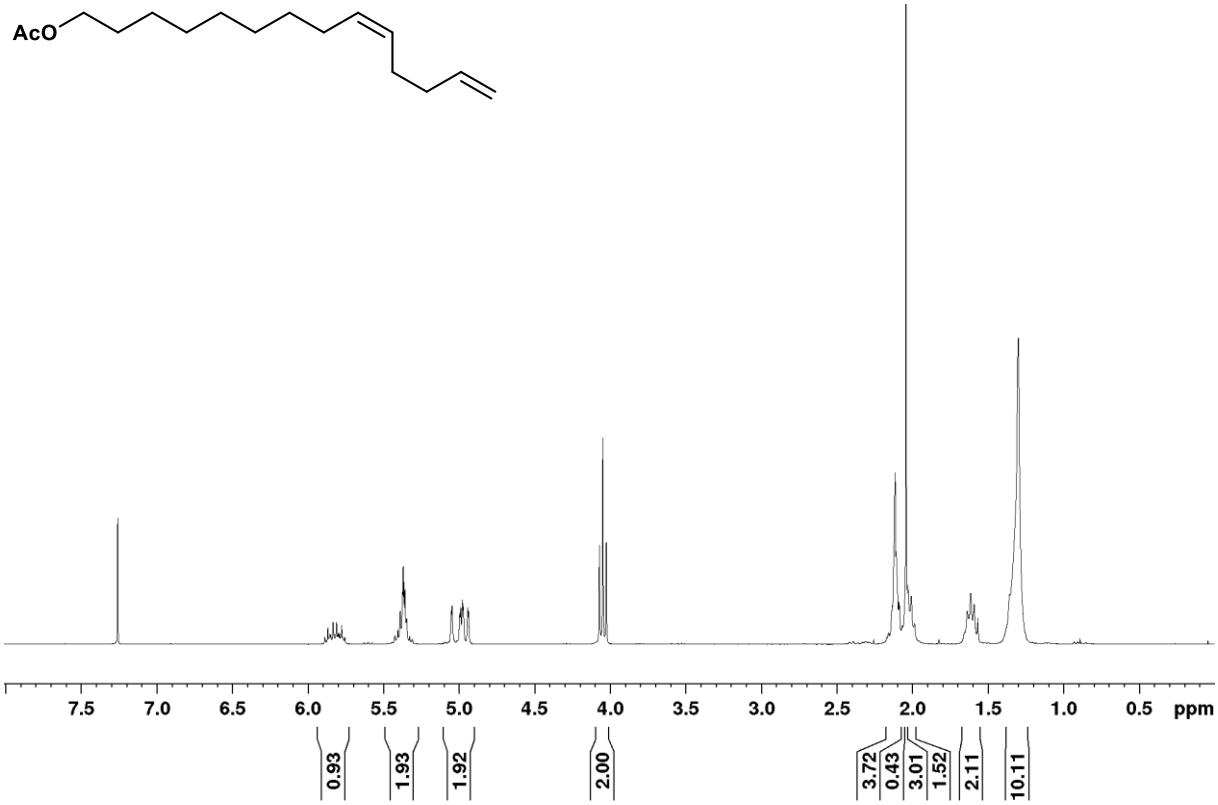


^{1}H NMR (300 MHz, $CDCl_3$).

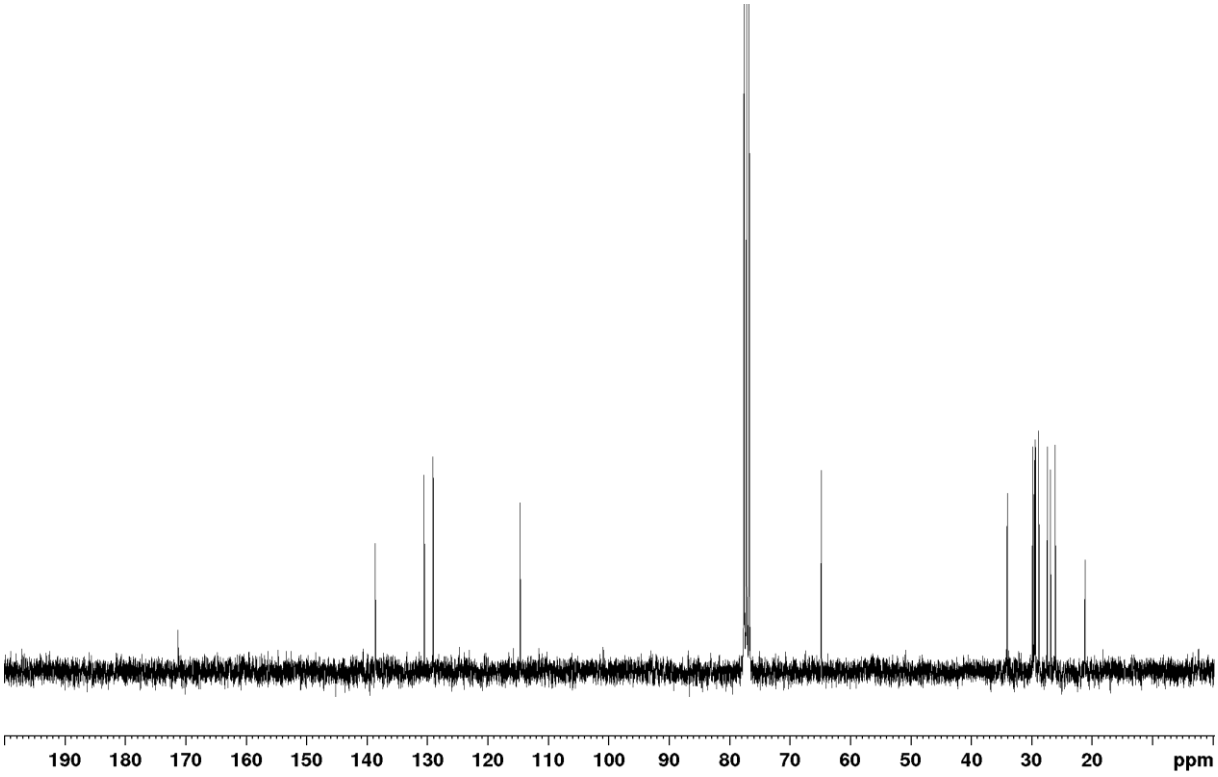


^{13}C NMR (75 MHz, $CDCl_3$).

(*Z*)-Tetradeca-9,13-dien-1-yl Acetate (184)

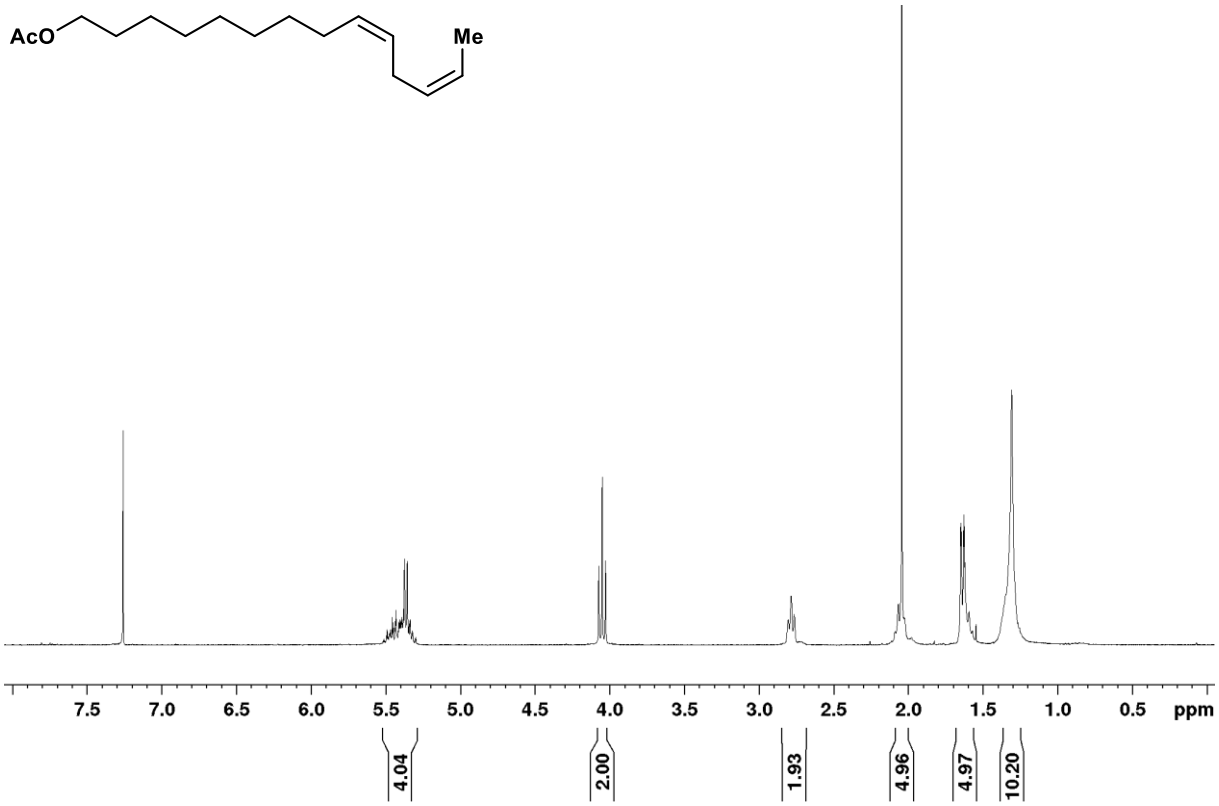


^{1}H NMR (500 MHz, $CDCl_3$).

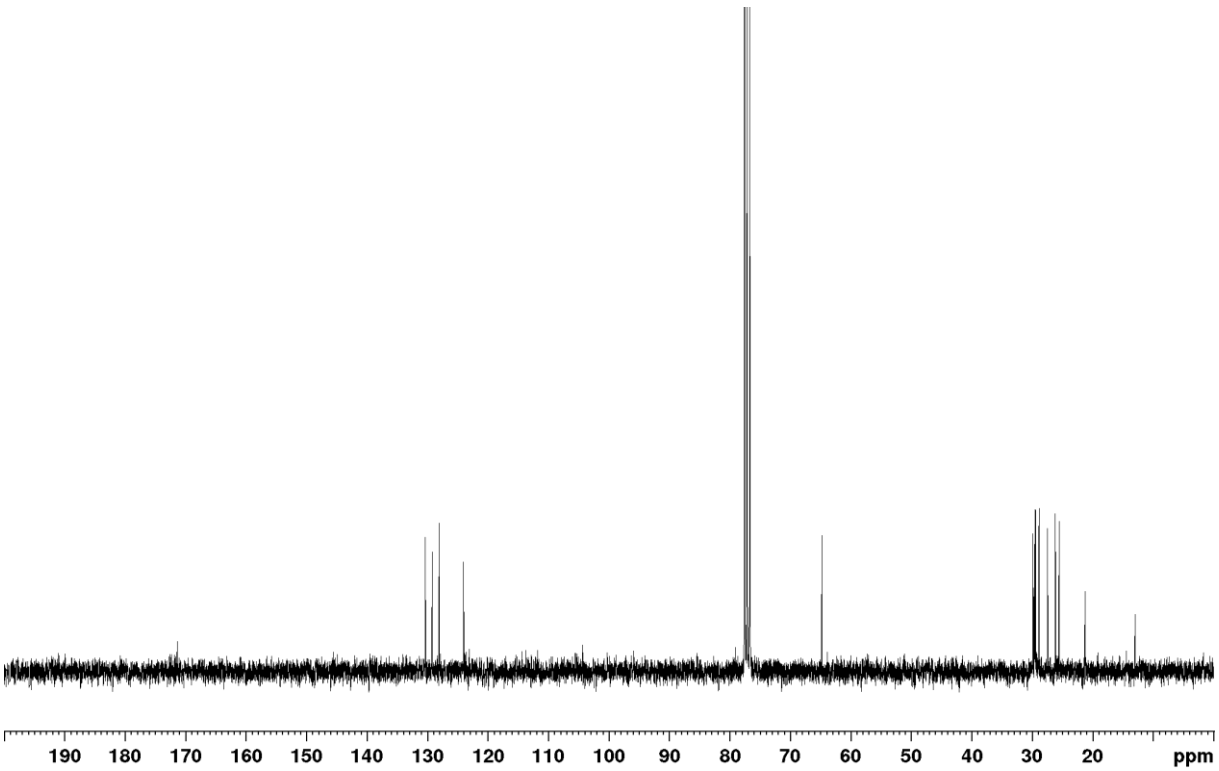


^{13}C NMR (75 MHz, $CDCl_3$).

(9*Z*,12*Z*)-Tetradeca-9,12-dien-1-yl Acetate (165)

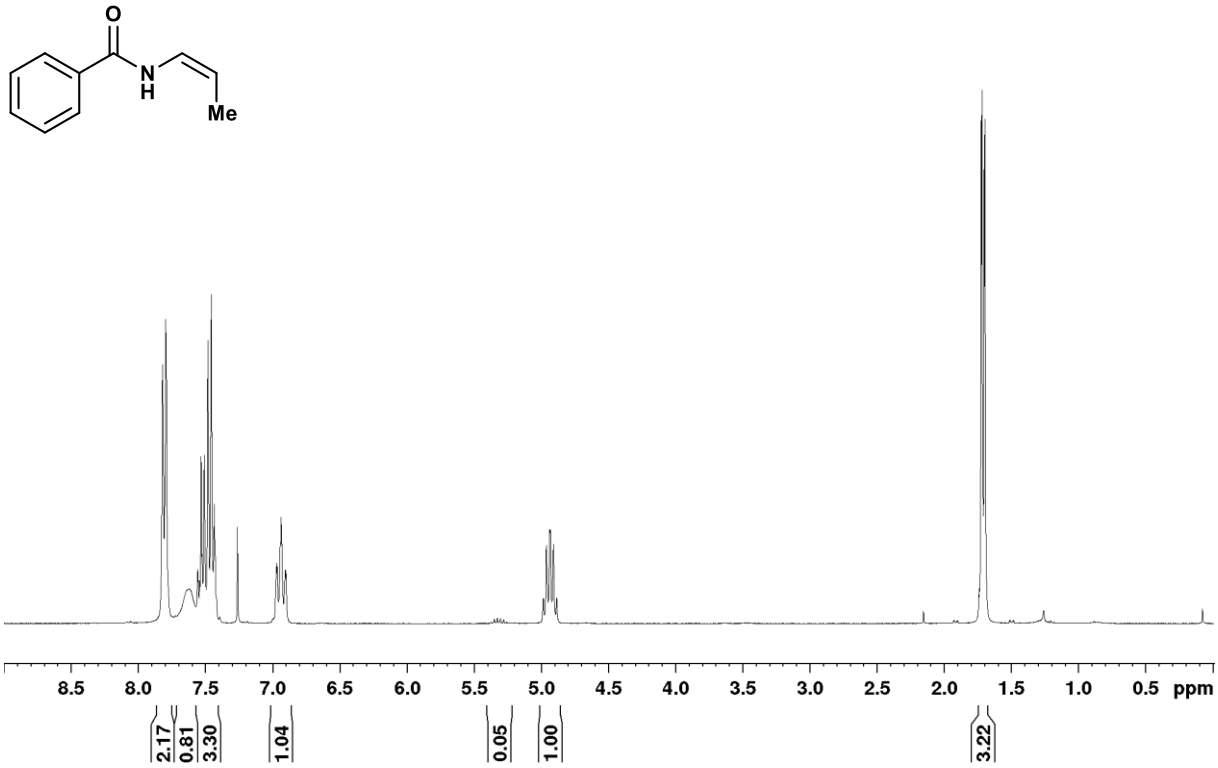


^{1}H NMR (300 MHz, $CDCl_3$).

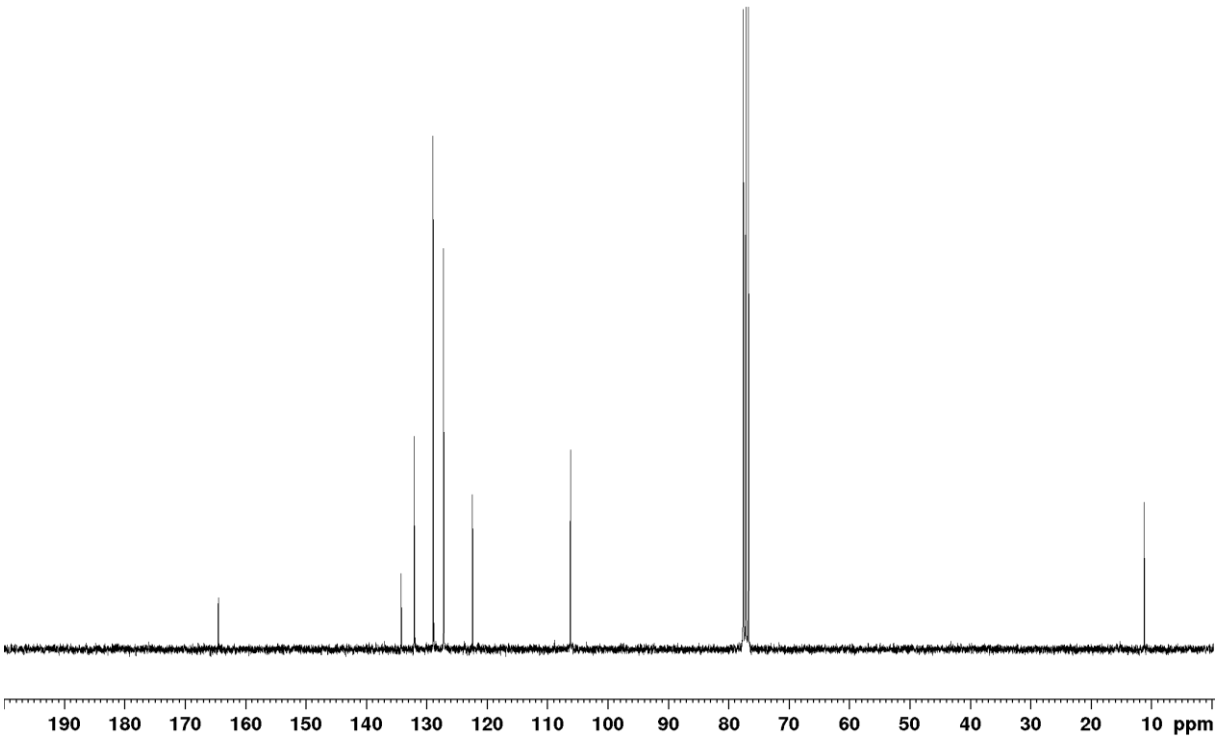


^{13}C NMR (75 MHz, $CDCl_3$).

(*Z*)-*N*-(Prop-1-en-1-yl)benzamide (72e)

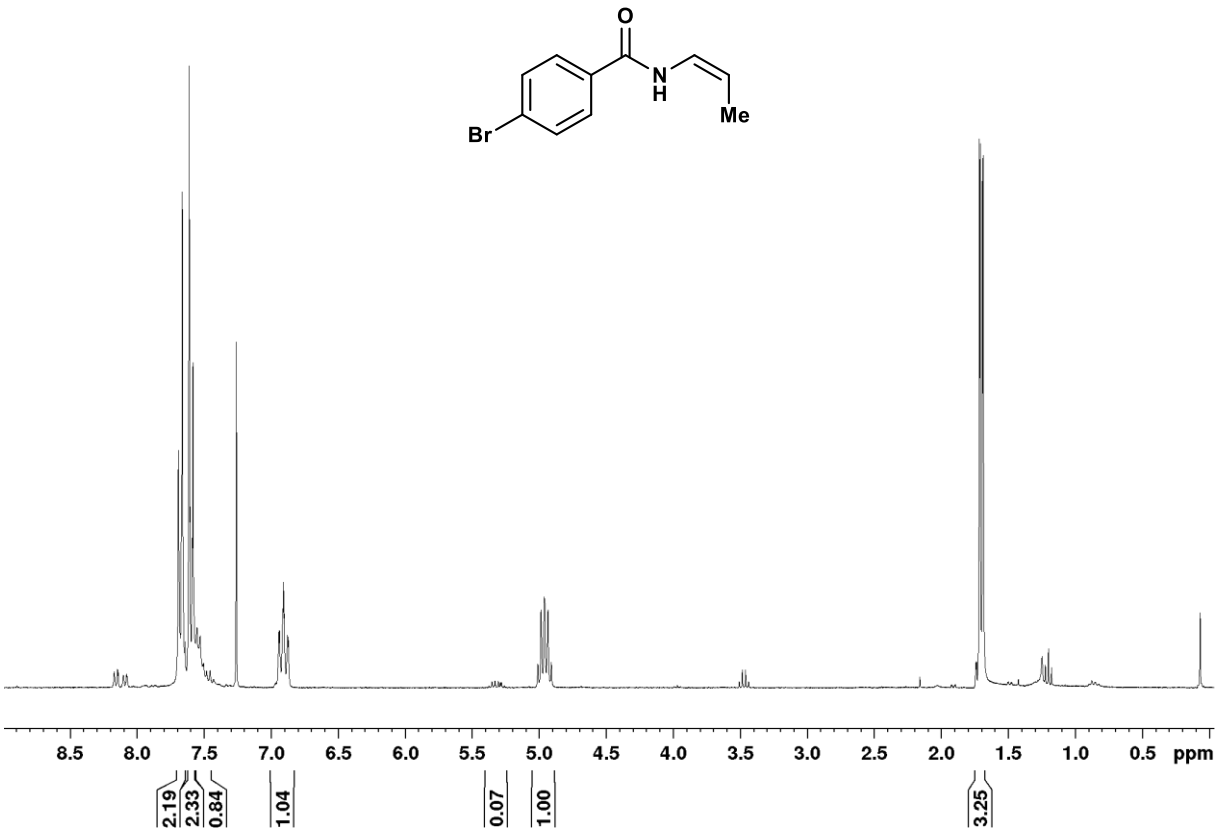


^{1}H NMR (300 MHz, $CDCl_3$).

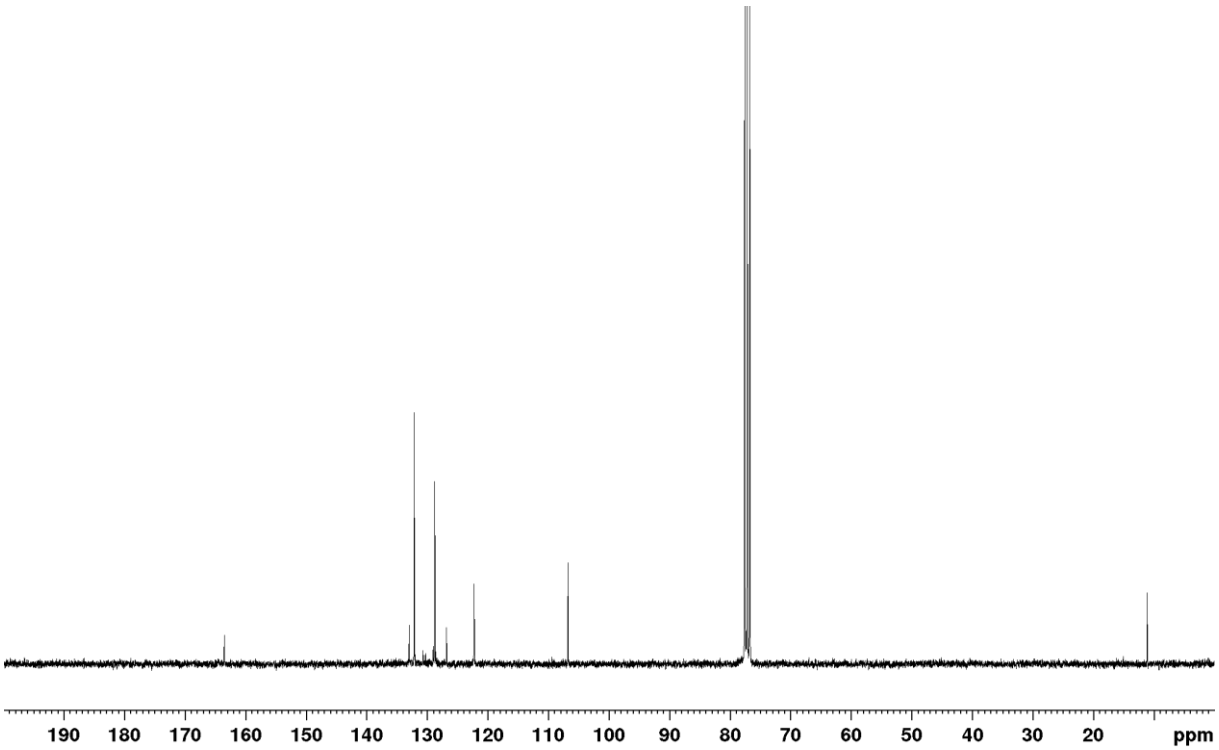


^{13}C NMR (75 MHz, $CDCl_3$).

(*Z*)-4-Bromo-*N*-(prop-1-en-1-yl)benzamide (72i)

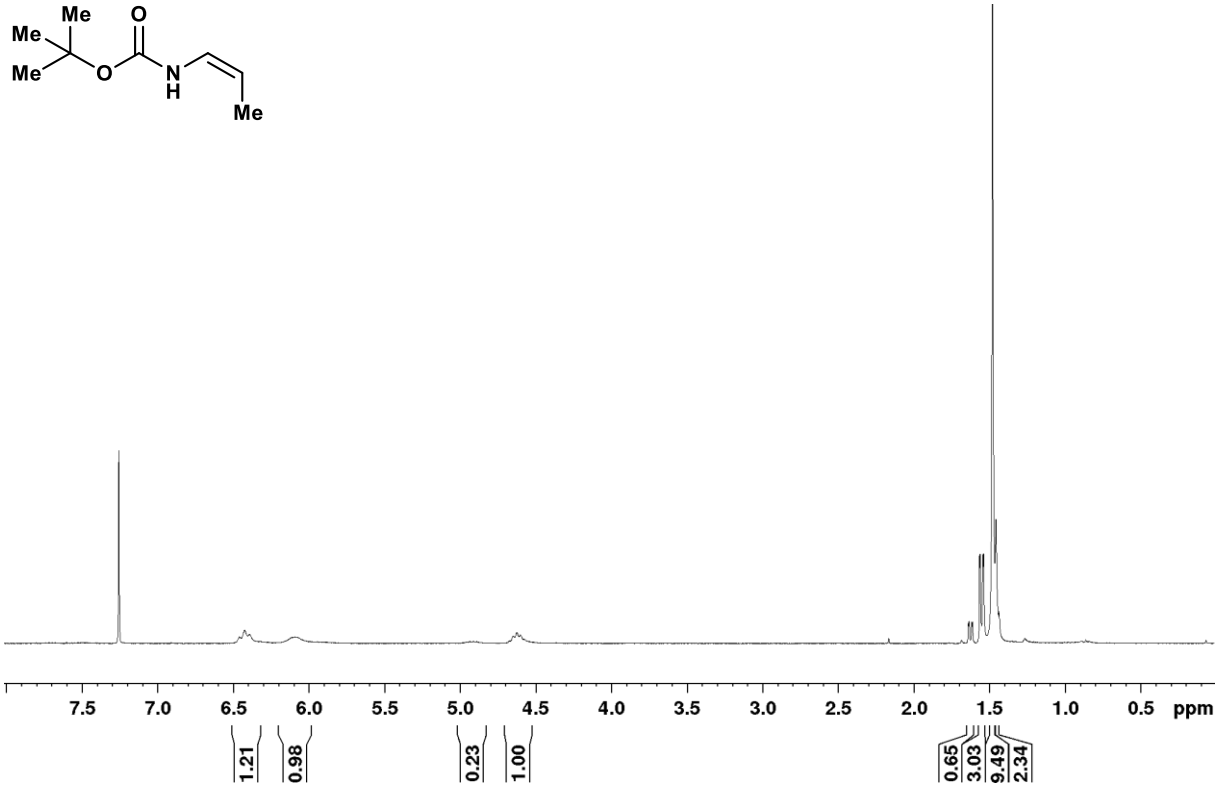


^{1}H NMR (300 MHz, $CDCl_3$).

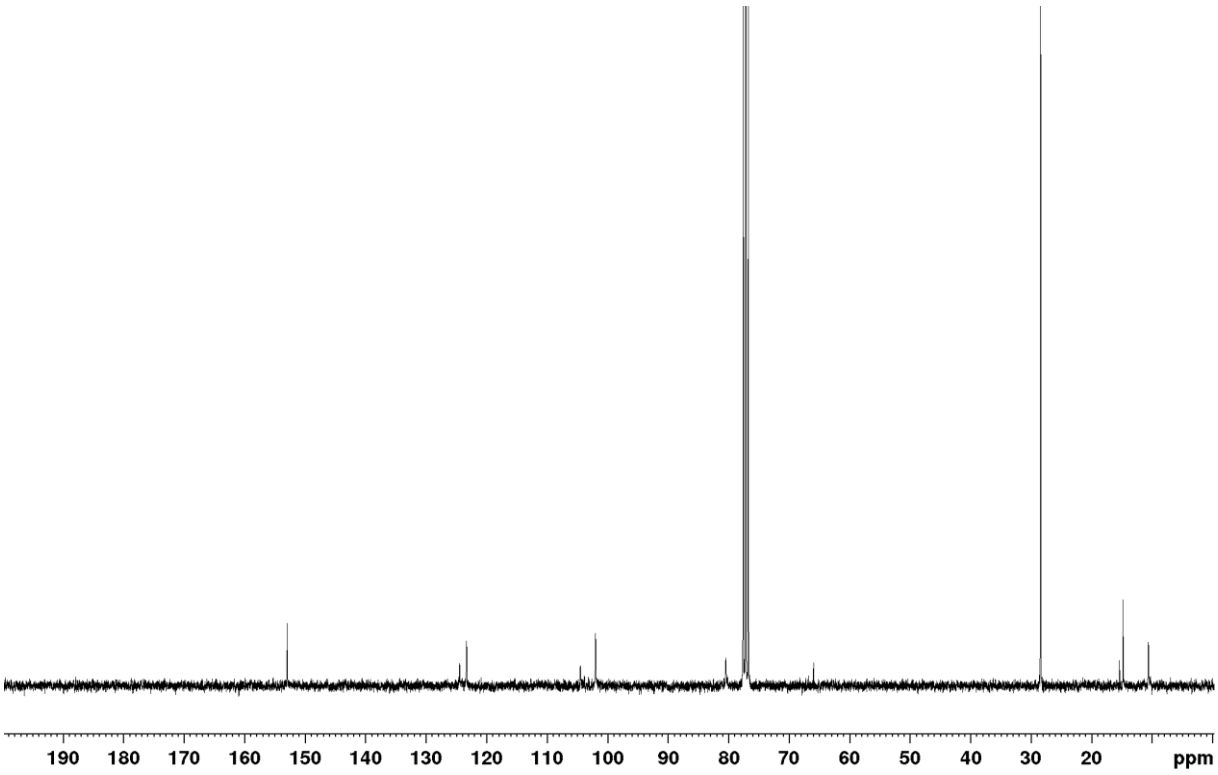


^{13}C NMR (75 MHz, $CDCl_3$).

tert-Butyl (_Z_)-prop-1-en-1-ylcarbamate (204a)

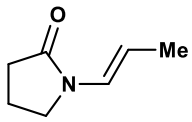


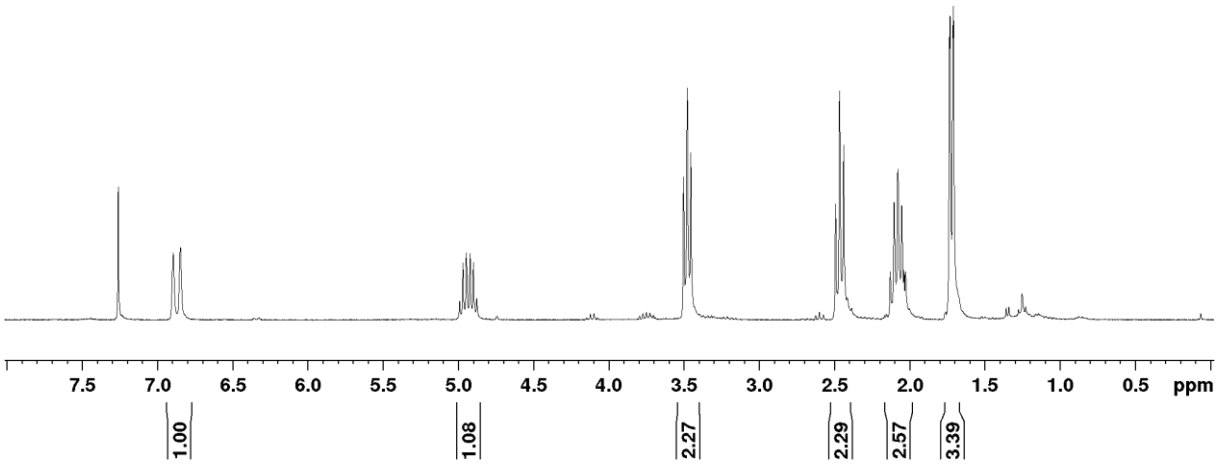
^{1}H NMR (300 MHz, $CDCl_3$).



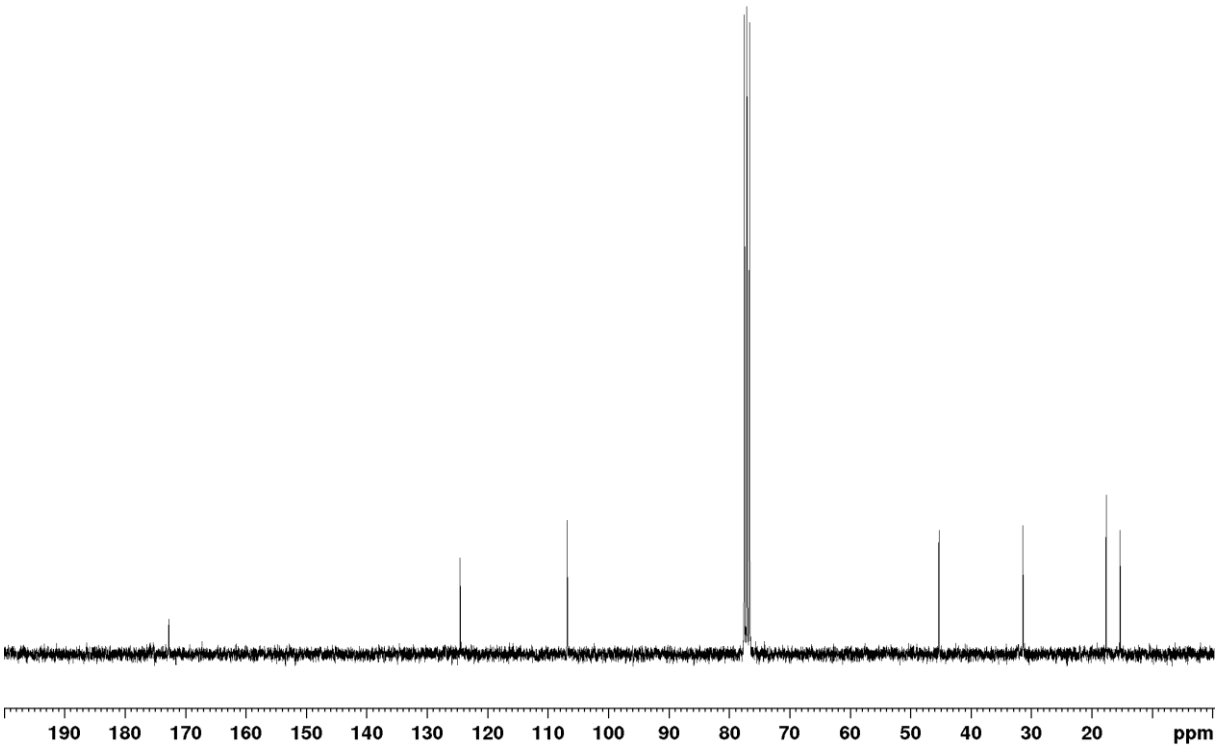
^{13}C NMR (75 MHz, $CDCl_3$).

(*E*)-1-(Prop-1-en-1-yl)pyrrolidin-2-one (210a)



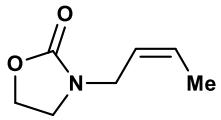


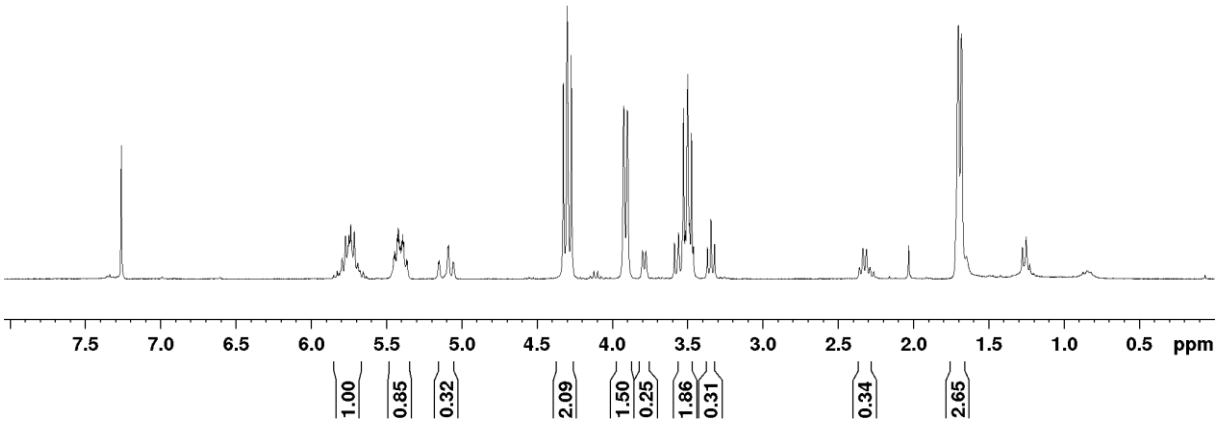
^{1}H NMR (300 MHz, $CDCl_3$).



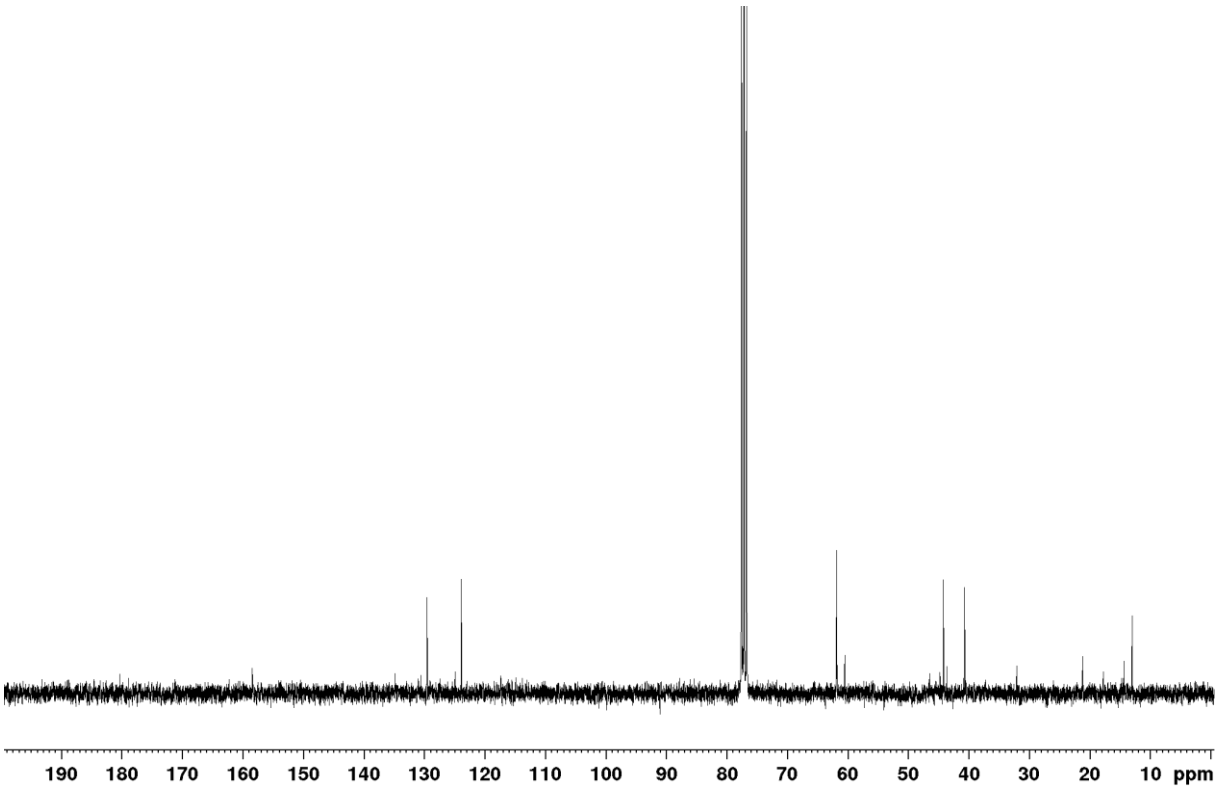
^{13}C NMR (75 MHz, $CDCl_3$).

(*Z*)-3-(But-2-en-1-yl)oxazolidin-2-one (219)



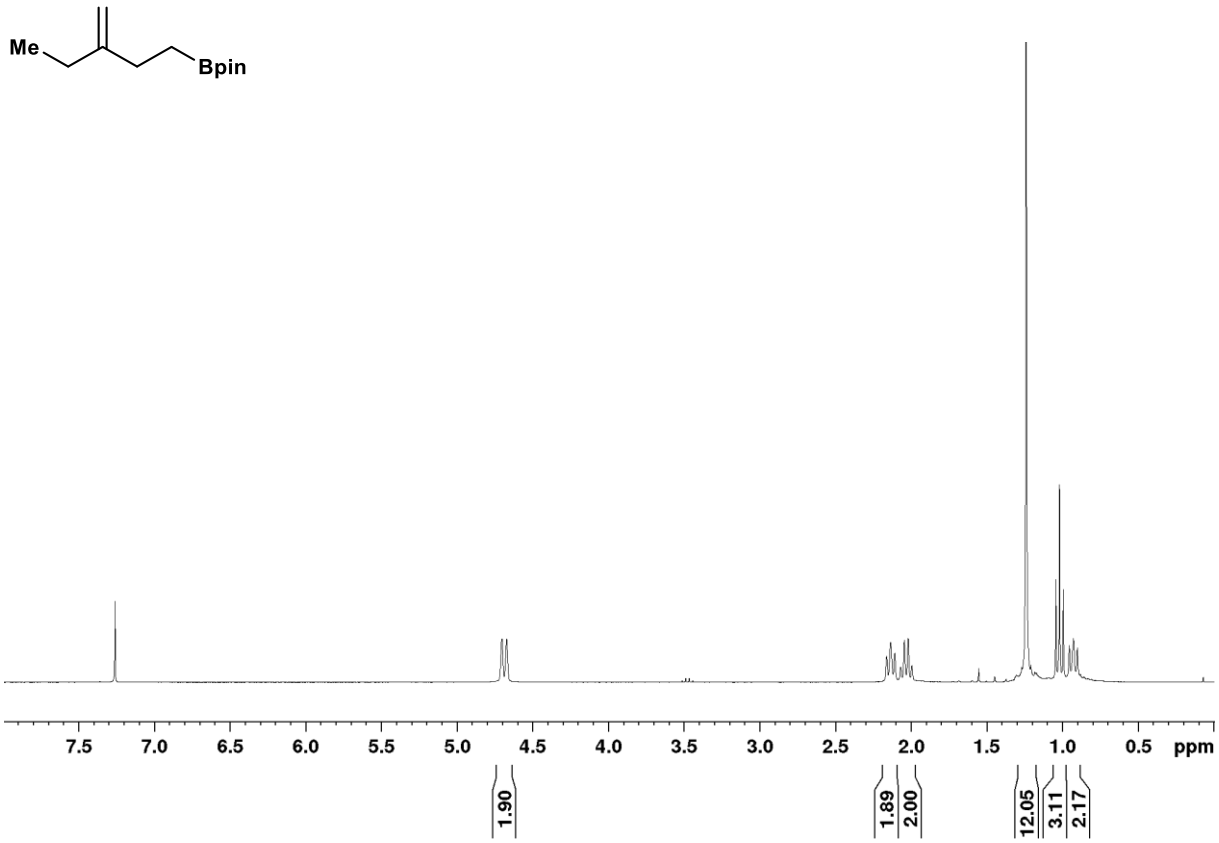


^{1}H NMR (300 MHz, $CDCl_3$).

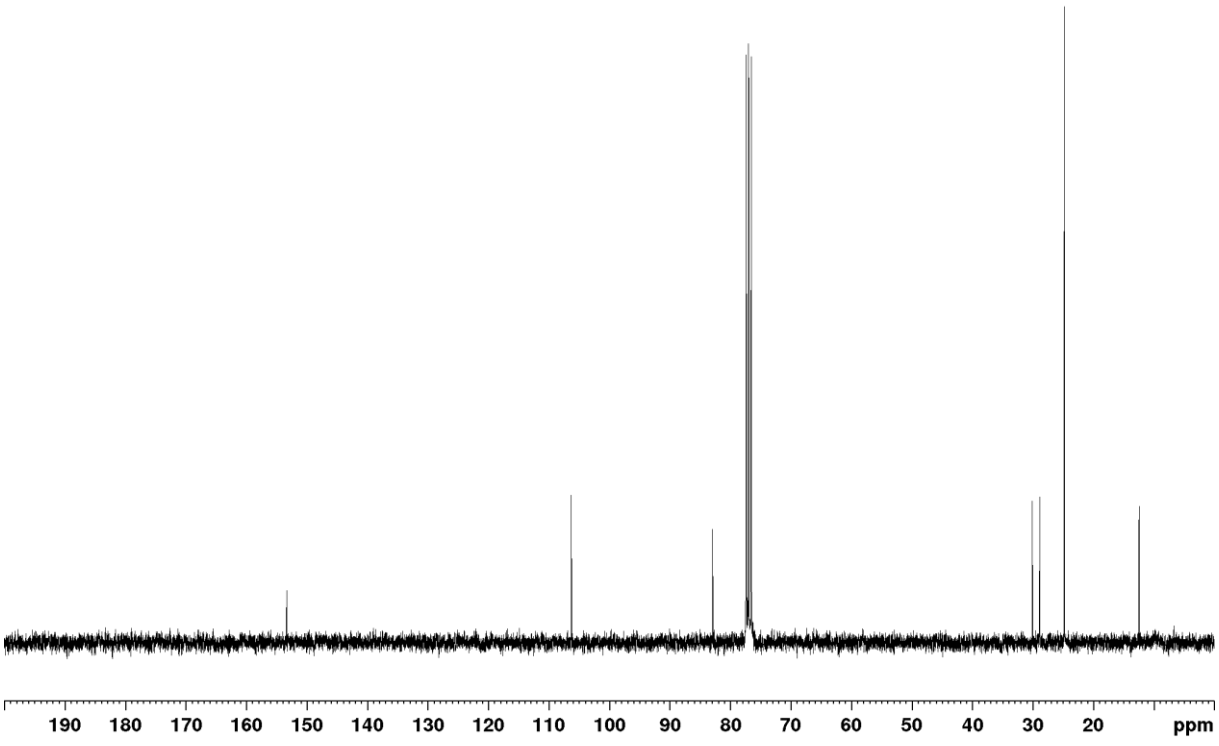


^{13}C NMR (75 MHz, $CDCl_3$).

4,4,5,5-Tetramethyl-2-(3-methylenepentyl)-1,3,2-dioxaborolane (231)

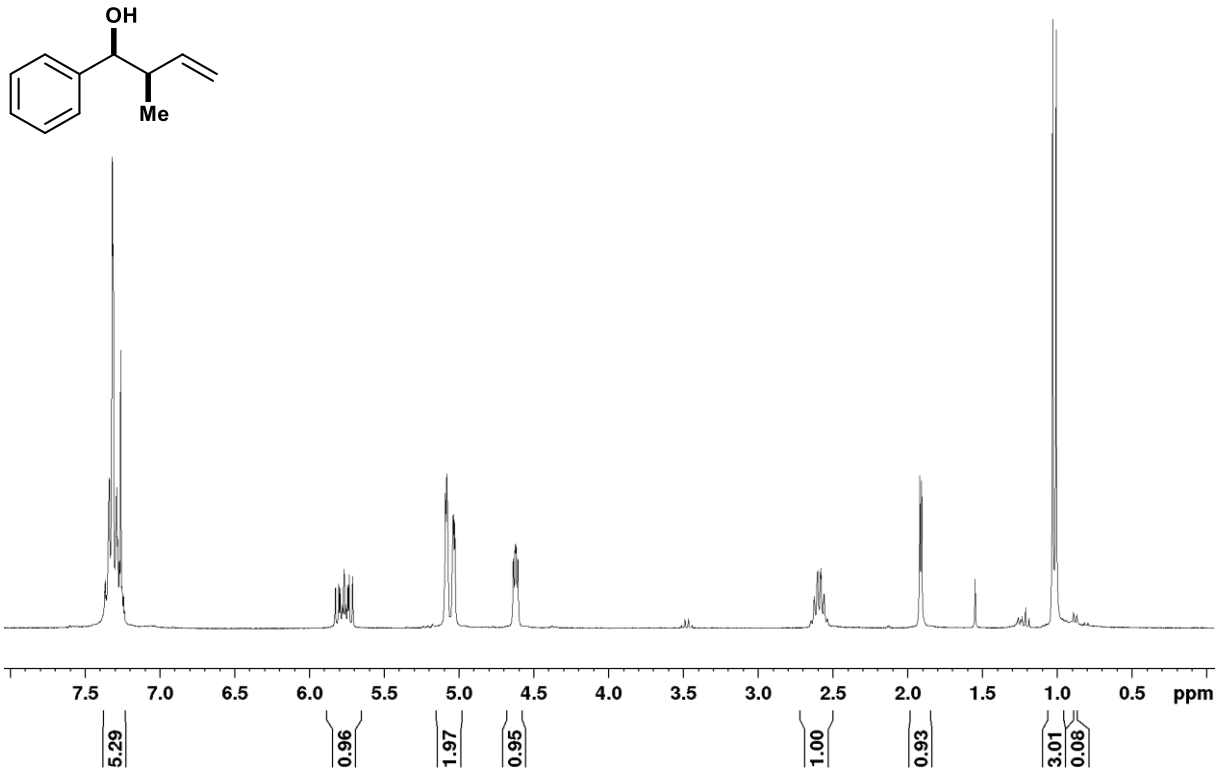


^{1}H NMR (300 MHz, $CDCl_3$).

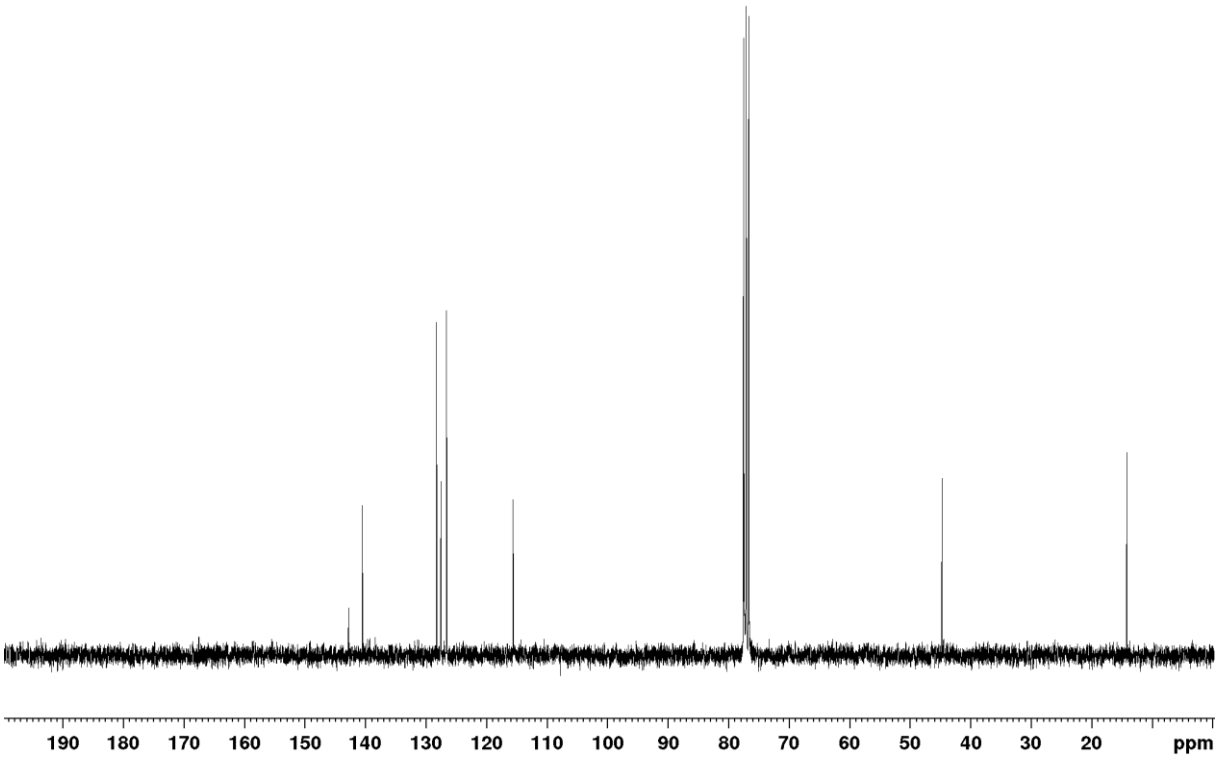


^{13}C NMR (75 MHz, $CDCl_3$).

***syn*-2-Methyl-1-phenylbut-3-en-1-ol (112)**

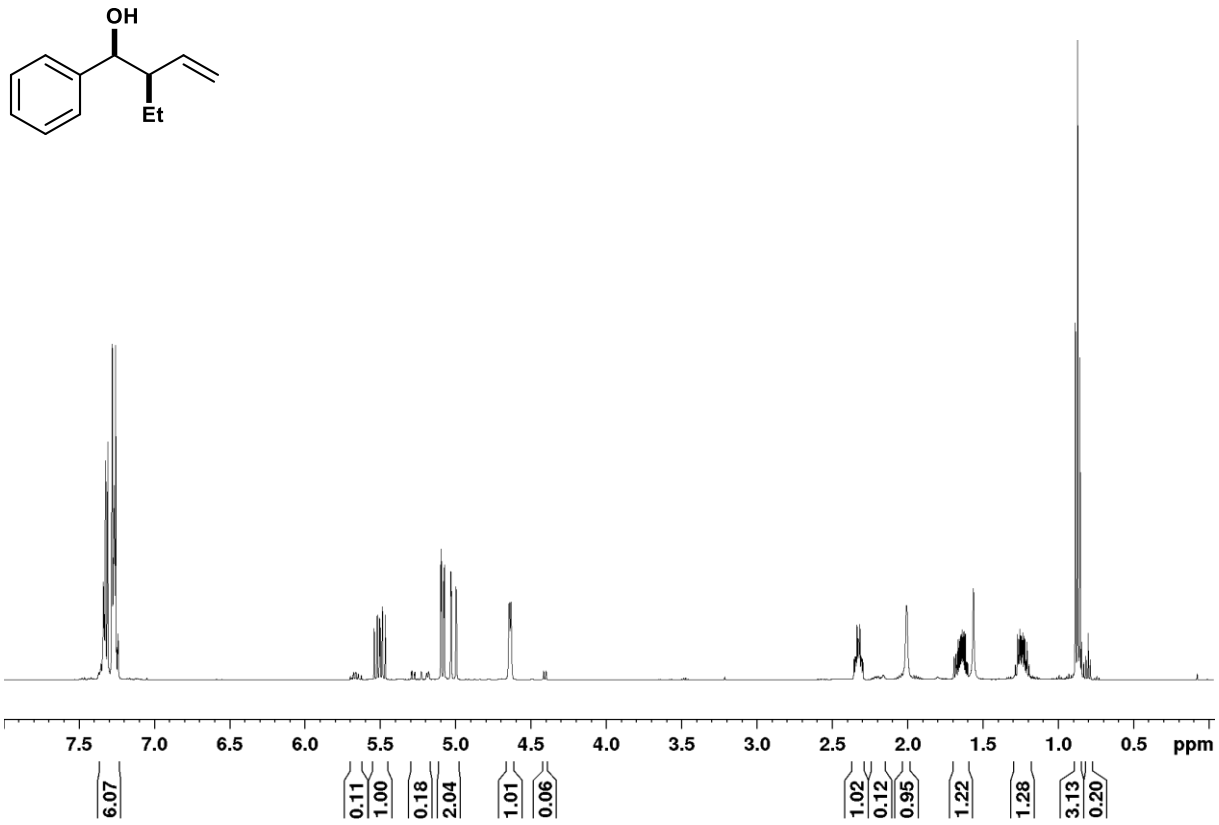


^{1}H NMR (300 MHz, $CDCl_3$).

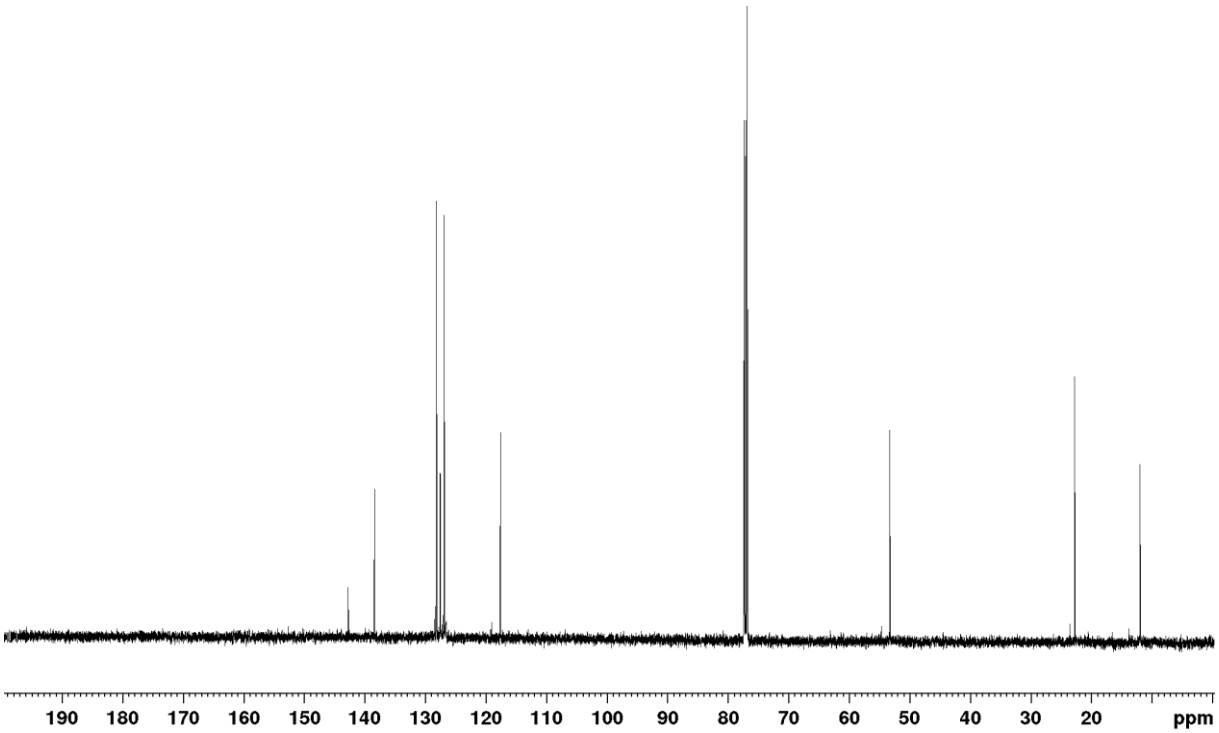


^{13}C NMR (75 MHz, $CDCl_3$).

***syn*-2-Ethyl-1-phenylbut-3-en-1-ol (237)**

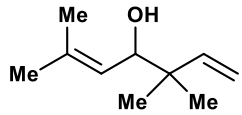


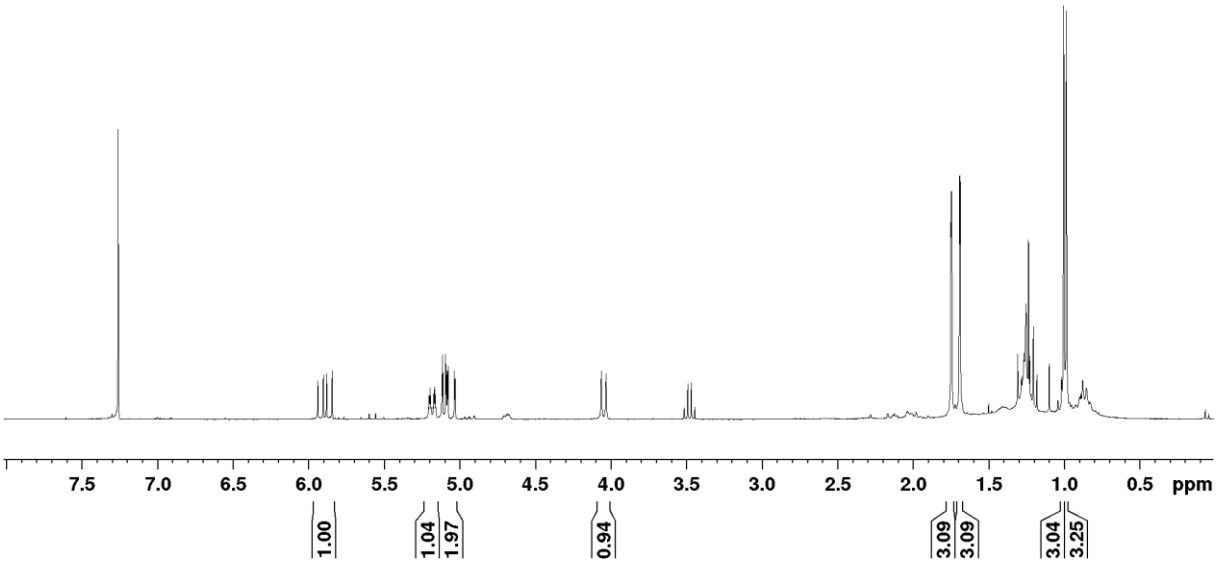
^{1}H NMR (300 MHz, $CDCl_3$).



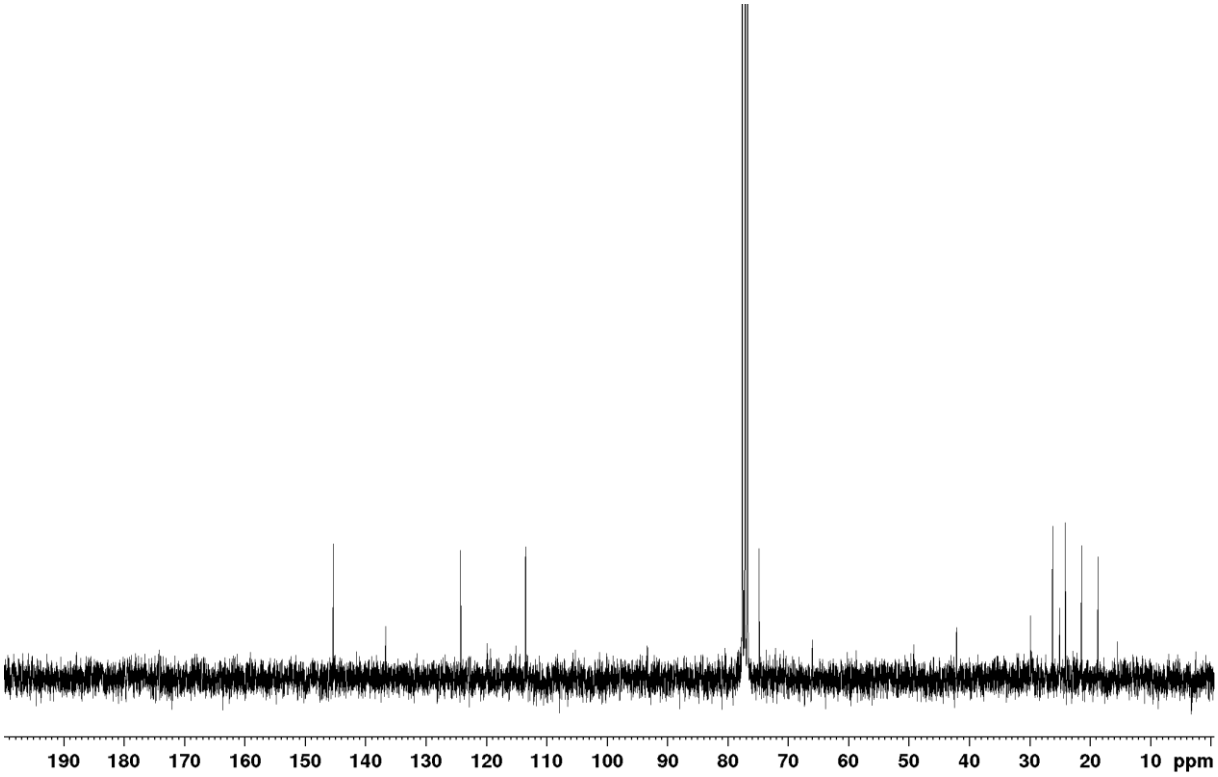
^{13}C NMR (125 MHz, $CDCl_3$).

Artemisia Alcohol (247c)



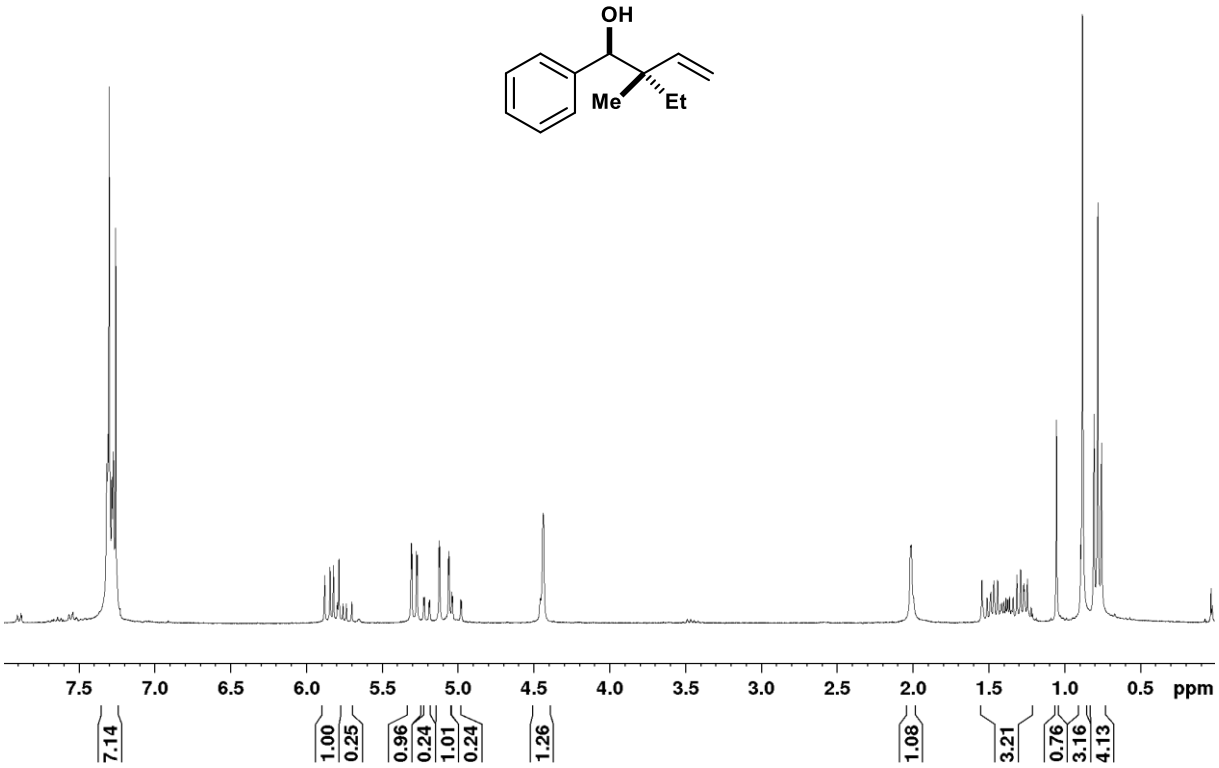


^{1}H NMR (300 MHz, $CDCl_3$).

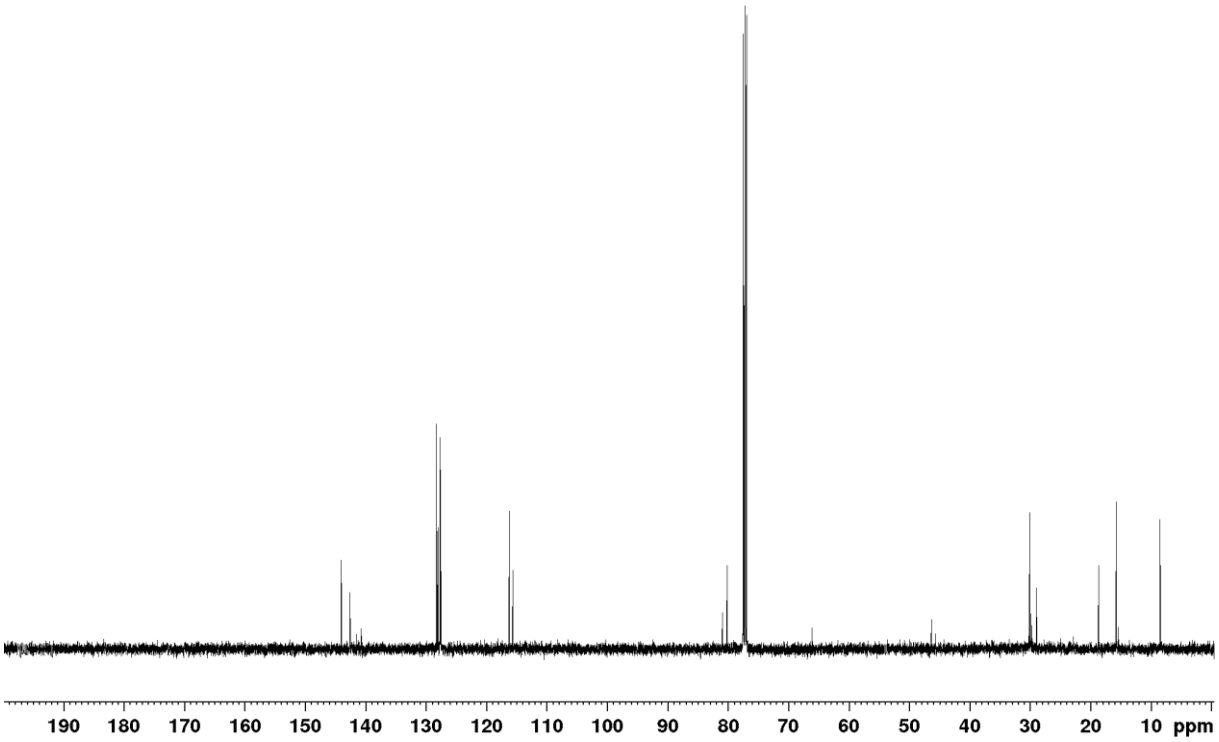


^{13}C NMR (75 MHz, $CDCl_3$).

***anti*-2-Ethyl-2-methyl-1-phenylbut-3-en-1-ol (130)**

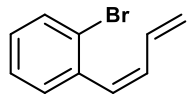


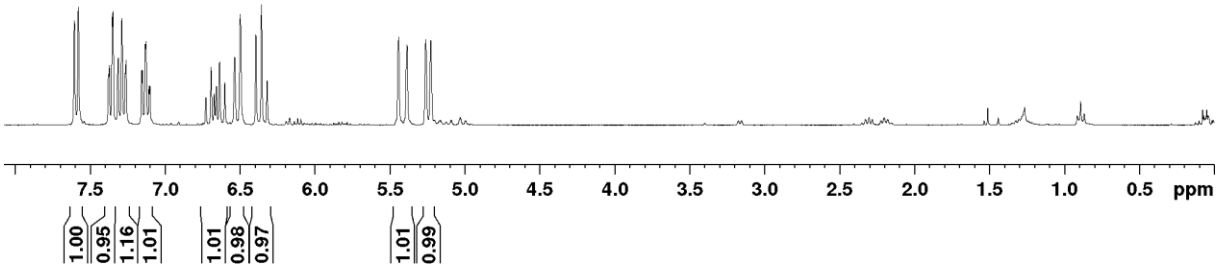
^{1}H NMR (300 MHz, $CDCl_3$).



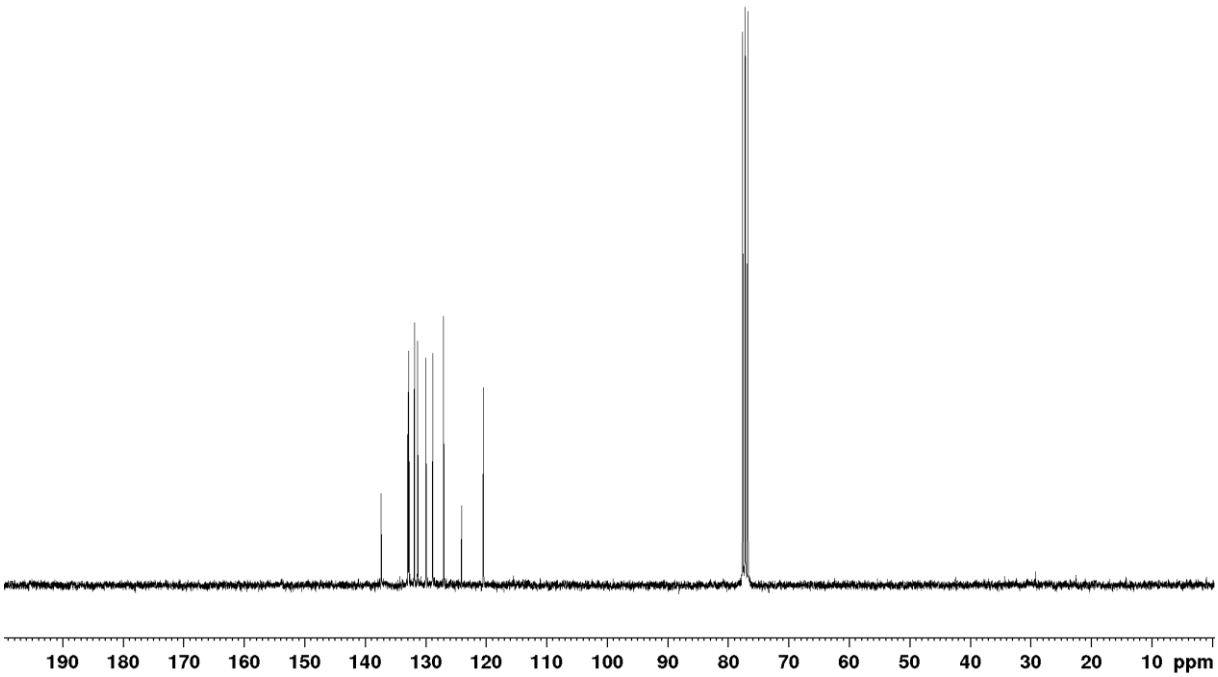
^{13}C NMR (125 MHz, $CDCl_3$).

(*Z*)-1-Bromo-2-(buta-1,3-dien-1-yl)benzene (273)



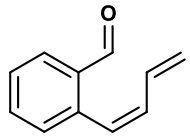


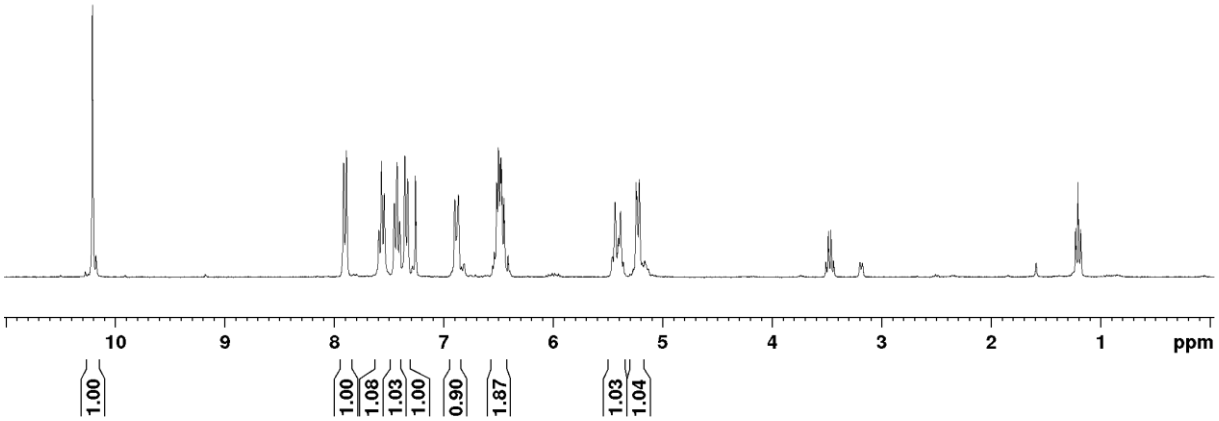
^{1}H NMR (300 MHz, $CDCl_3$).



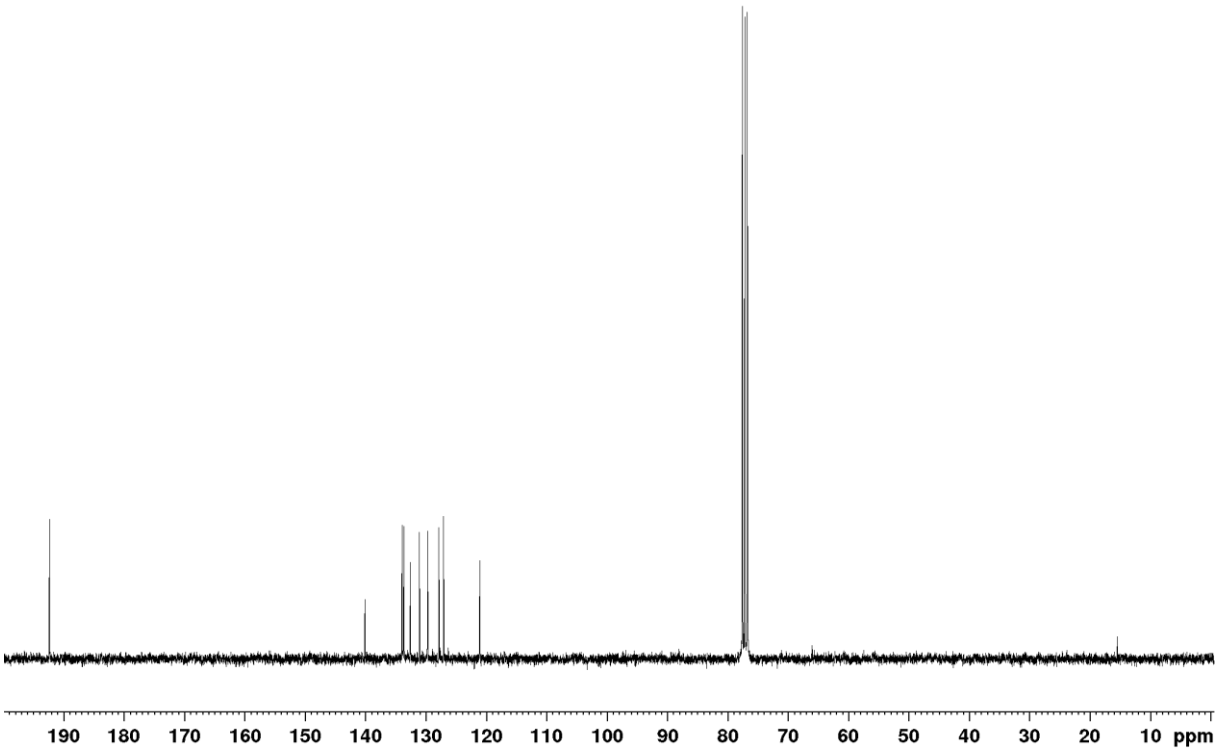
^{13}C NMR (75 MHz, $CDCl_3$).

(*Z*)-2-(Buta-1,3-dien-1-yl)benzaldehyde (262)



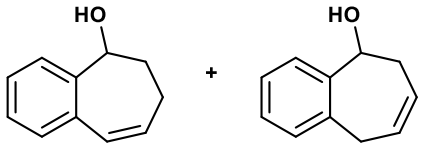


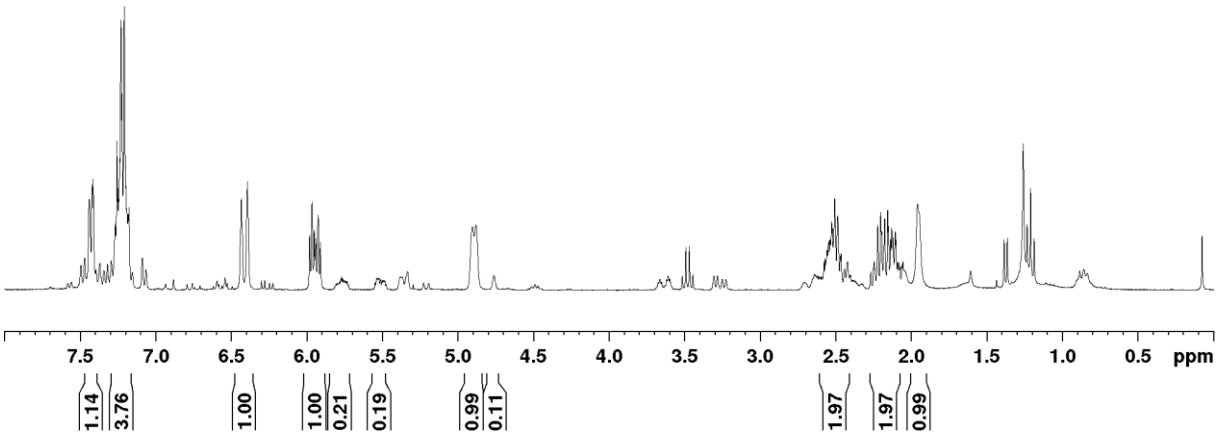
^{1}H NMR (300 MHz, $CDCl_3$).



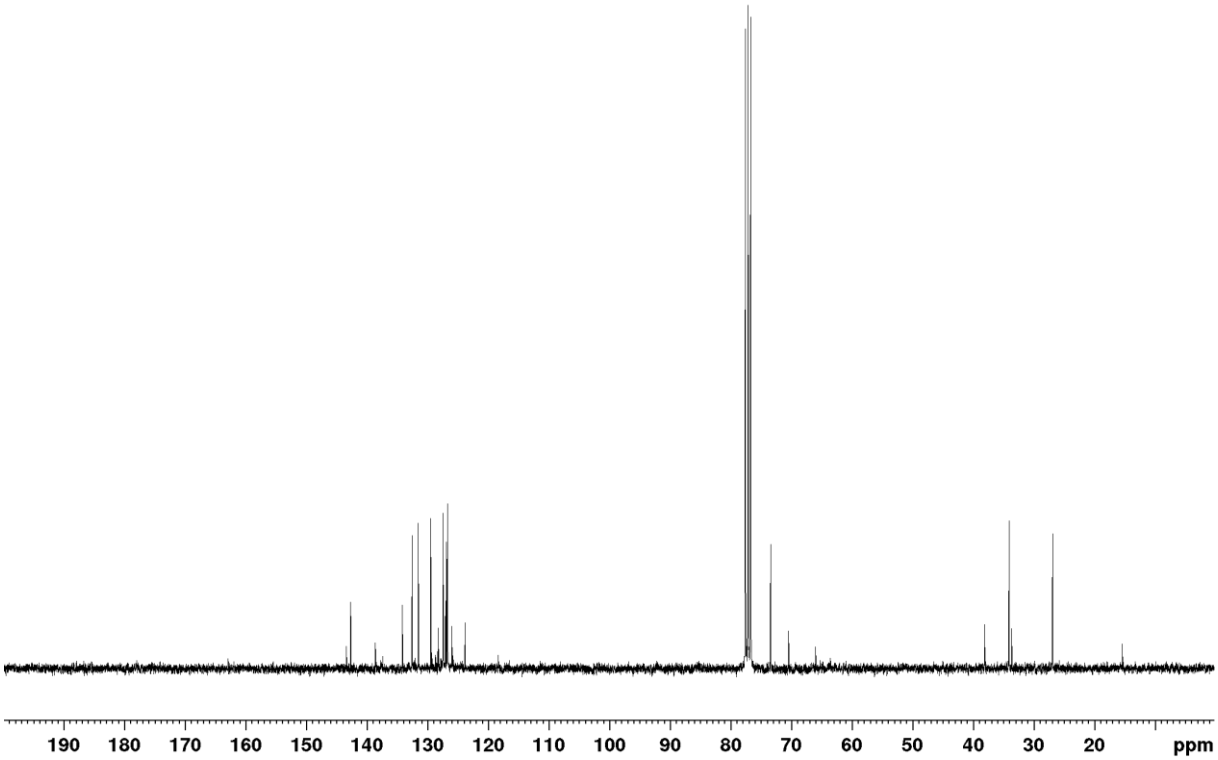
^{13}C NMR (75 MHz, $CDCl_3$).

6,7-Dihydro-5*H*-benzo[7]annulen-5-ol (266) and 6,9-Dihydro-5*H*-benzo[7]annulen-5-ol (266‘)





^{1}H NMR (300 MHz, $CDCl_3$).



^{13}C NMR (125 MHz, $CDCl_3$).

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